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(57) Abstract

The functional domains of Elongin A having transcriptional activation activity and Elongin BC binding activity and the functional domains of Elongin C having Elongin A activation activity and Elongin A and/or Elongin C binding activity have now been identified and isolated.

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ELONGIN A AND C FUNCTIONAL DOMAINS

TECHNICAL FIELD OF THE INVENTION

The invention relates to the identification and characterization of the functional domains of the subunits of the elongation factor Elongin required for transcriptional activation of RNA Polymerase II and the regulation thereof.

BACKGROUND OF THE INVENTION

Transcription is the synthesis of a strand of RNA representing or complementary to the coding strand of a DNA duplex. It takes place by the usual process of complementary base pairing and is catalyzed by the enzyme RNA polymerase. Transcription is the first step in the expression of a gene and it is the principle step at which gene expression is controlled or regulated.

The transcription process can be controlled at any one of the three stages of transcription: initiation, elongation, or termination. In eukaryotic systems, initiation involves the association of the RNA polymerase with several other enzymes and factors at the promoter. For accurate initiation, a number of the specific initiation factors are required.

Elongation is the phase in which the RNA polymerase moves along the strand of DNA, extending the growing RNA chain as it does so. As the RNA polymerase moves it unwinds the DNA helix to expose a new segment of the template in single-stranded form. Nucleotides are then covalently added to the 3' end of the elongating RNA chain forming an RNA-DNA hybrid in the unwound region. The DNA strand then re-associates with its DNA complement, thereby reforming the double helix structure and displacing the single-stranded RNA strand. Thus, elongation involves the transient disruption of DNA structure to form an unwound region that exists as a hybrid RNA-DNA duplex and a displaced single strand of DNA.

Termination of transcription occurs when the RNA polymerase reaches a termination codon, i.e., a noncoding segment of the DNA template strand. At this point, no additional nucleotides are added to the RNA chain. The termination stage ends when the RNA polymerase, DNA template, and newly synthesized RNA chain dissociate into separate entities.

Messenger RNA (mRNA)transcription is a complex bio-chemical process requiring the action of multiple transcription factors. Transcription factors include both initiation and elongation factors, which control the activity of the RNA polymerase at the initiation and elongation stages of transcription, respectively. Several of these factors are known to be essential for initiation and are referred to as factors D, E, A, G, and B from *Saccharomyces cerevisiae*, τ, α, βγ, δ, and ε from rat liver, and TFIID, TFIIB, RAP30/74 or TFIIF, BTF2 or TFIIH, and TFIIE from human cells.

In addition to these factors, other proteins have been shown to stimulate either the initiation or elongation stages of transcription by RNA Polymerase II. One such factor, designated TFIIA, has been purified from both *Saccharomyces cerevisiae* and mammalian cells. TFIIA appears to promote assembly of the transcriptional pre-initiation complex. Although TFIIA is not essential for initiation, several lines of evidence suggest that it functions to increase the number of pre-initiation complexes that form at the promoter.

Considerable progress has recently been achieved identifying and characterizing transcriptional factors that support a basal level of transcription by RNA Polymerase II. Significantly less information, however, is available on transcription factors regulating the efficiency of transcriptional initiation or RNA chain elongation. Such transcriptional factors play an important role in regulating gene expression.

Currently, five general transcription elongation factors influencing RNA chain elongation have been identified and characterized with a high degree of certainty. These are SII, P-TEFb, TFIIF, ELL, and Elongin (also known as "SIII"). The general elongation factors TFIIF (RAP30/74) and ELL act to increase the overall rate of RNA chain elongation by suppressing transient pausing of the RNA polymerase at a variety of sites. The transcription factors SII and P-TEFb prevent RNA Polymerase II from arresting transcription prematurely. SII has been shown to promote RNA polymerase read-through at intrinsic pause sites in a human histone gene, the adenyl virus genome, and at several other sites. SII is a 38 kiloDalton (kD) elongation factor that promotes passage of RNA Polymerase II through transcriptional impediments such as nucleoprotein complexes and DNA sequences acting as intrinsic arrest sites. P-TEFb catalyzes the conversion of early, termination prone elongation complexes into productive elongation complexes.

A fifth elongation factor which increases the overall rate at which RNA Polymerase II transcribes DNA

is Elongin. Elongin is a trimeric complex consisting of three protein subunits labeled Elongin A (110 kD as measured by SDS-PAGE), Elongin B (18 kD as measured by SDS-PAGE), and Elongin C (15 kD as measured by SDS-PAGE) having 773, 118 and 112 amino acid residues, respectively. Elongin A is capable of weakly stimulating transcriptional activity at a low level in the absence of Elongin B and/or C, while Elongins B and C serve regulatory functions which increase the transcriptional activation activity of Elongin A. Elongins B and C bind stably to each other in the absence of Elongin A to form a binary complex (Elongin BC) that interacts with Elongin A strongly inducing its transcriptional activity.

In addition, it has been shown that Elongin C can assemble with Elongin A in the absence of Elongin B to form an Elongin AC complex which increased specific activity, thereby increasing the rate of RNA chain elongation. Elongin B does not interact with Elongin A in the absence of Elongin C and apparently functions like a chaperone protein facilitating the assembly and enhancing the stability of the Elongin ABC complex. The identification, purification and characterization of Elongin and its subunits Elongins A, B and C have been described in U.S. Serial No. 08/524,757 filed on September 7, 1995, and incorporated herein by reference.

Elongin has also been reported to interact with the product ("pVHL") of the Von Hippel-Lindau tumor suppressor gene. The Von Hippel-Lindau tumor

suppressor gene, which predisposes individuals to various tumor types, translates into a 213 amino acid protein capable of binding to and inhibiting the activity of Elongin. In particular, it has been reported that wild-type pVHL binds tightly and specifically to the Elongin BC complex and prevents it from activating Elongin A. That is, binding of the pVHL protein and Elongin A to the Elongin BC complex are mutually exclusive *in vitro*.

The previous work on Elongin described above provided a useful product for regulating the transcriptional activity of RNA Polymerase II. There still remained, however, a need to identify the functional domains of the Elongin subunits. As described herein, the Elongin A transcriptional activation domain has now been identified. This domain has been found to define a new evolutionarily conserved class of inducible activation domain. It has also been shown that the transcriptional activation domain of Elongin A and the Von Hippel-Lindau tumor suppressor protein (pVHL) interact with the Elongin BC complex through a conserved Elongin BC binding site motif essential for induction of Elongin A activity by Elongin BC and for tumor suppression by the VHL protein. In addition, the regions of Elongin C important for binding to Elongin B and for binding to and activating Elongin A have also been identified.

The identification and characterization of these domains serves two purposes. First, Elongin subunits or fragments thereof having at least the functional

domains described herein can be used in place of the entire subunits in *in vitro* transcriptional assays or systems. Secondly, and perhaps more importantly, these regions can be used as laboratory reagents for work concerning the transcriptional activation activities of Elongin.

SUMMARY OF THE INVENTION

The present invention relates to the domains of Elongin A having transcriptional activation activity and Elongin BC binding activity. In another aspect, the present invention relates to an analog of the human Elongin A.

In another aspect, the present invention relates to the domains of Elongin C having Elongin activation activity and Elongin A and/or Elongin B binding activity.

In still another aspect, the present invention relates to the nucleotide sequences encoding the various Elongin subunits and their functional domains.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1A. N- and C-terminal Elongin A deletion mutants analyzed in this study. At right, the results of assays described in the text and shown in panels 1C and 1D are summarized. N.D., not determined.

Fig. 1B. Wild type Elongin A was refolded together with wild type Elongin B and C and subjected to TSK SP-NPR HPLC as described. Aliquots of column fractions were analyzed by SDS-PAGE, and proteins were visualized by silver staining. M, molecular weight markers; L, load; FT, flow through; kDa, kilodaltons; A, Elongin A; B, Elongin B; C, Elongin C.

Fig. 1C. N- and C-terminal Elongin A deletion mutants were refolded together with wild type Elongin B and C and subjected to TSK SP-NPR HPLC as described. Aliquots containing ~100 ng of the peak column fractions were analyzed by SDS-PAGE, and proteins were visualized by silver staining. In this and subsequent figures, WT designates wild type Elongin A.

Fig. 1D. Runoff transcription assays were performed as described. Reaction mixtures in lanes 1 and 10 contained no Elongin. Elongin complexes were present in reaction mixtures at the indicated relative molar concentrations; a relative molar concentration of 1 is equivalent to ~2 nM Elongin A. In this and subsequent figures, AdML indicates the position of the full-length ~250 nucleotide runoff transcript synthesized by RNA Polymerase II from the AdML promoter.

Fig. 2A. Analysis of Elongin A internal deletion mutants. At right, the results of assays described in the text and shown in panels 2B and 2C are summarized.

Fig. 2B. Elongin A internal deletion mutants were refolded together with wild type Elongin B and C and subjected to TSK SP-NPR HPLC as described. Aliquots containing ~100 ng of the peak column fractions were analyzed by SDS-PAGE, and proteins were visualized by silver staining.

Fig. 2C. Runoff transcription assays were performed as described. Elongin complexes were present in reaction mixtures at the indicated relative molar concentrations; a relative molar concentration of 1 is equivalent to ~2 nM Elongin A.

Fig. 3A. Analysis of short Elongin deletion mutants containing the minimal transcriptional activation domain. Elongin A deletion mutants were refolded together with wild type Elongin B and C and subjected to TSK SP-NPR HPLC as described. Aliquots containing ~100 ng of the peak column fractions were analyzed by SDS-PAGE, and proteins were visualized by silver staining.

Fig. 3B. Runoff transcription assays were performed as described. The reaction mixture in lane 1 contained no Elongin. Elongin complexes were present in reaction mixtures at the indicated relative molar concentrations; a relative molar concentration of 1 is equivalent to ~2 nM.

Fig. 4A. Analysis of Elongin A internal deletion mutants with mutations in the potential Elongin BC

binding site. At the top is shown a comparison of the similar regions of Elongin A and the VHL protein. The portion of the VHL protein shown to be sufficient for binding to Elongin B and C (Kibel et al. 1995) is underlined; vertical lines indicate identical amino acids; colons indicate chemically similar amino acids. *Elo*A, Elongin A; *VHL*, VHL protein.

Fig. 4B. Elongin A internal deletion mutants were refolded together with wild type Elongin B and C and subjected to TSK SP-NPR HPLC as described. Aliquots containing ~100 ng of the peak column fractions were analyzed by SDS-PAGE, and proteins were visualized by silver staining.

Fig. 5A. Transcription activity of Elongin A internal deletion and point mutants with mutations in the potential Elongin BC binding site. Runoff transcription assays were performed as described. Elongin complexes were present in reaction mixtures at the indicated relative molar concentrations; a relative molar concentration of 1 is equivalent to ~2 nM Elongin A.

Fig. 5B. Runoff transcription assays were performed as described in the absence and presence of excess wild type Elongin BC. Runoff transcription assays were performed in the presence of 4 nM TSK SP-NPR purified Elongin complexes of the indicated relative molar concentrations of purified Elongin BC complex; a relative molar concentration of 1 is equivalent to ~4 nM Elongin BC. BC, purified Elongin BC complex.

Fig. 6. Naturally occurring VHL mutants and synthetic Elongin A point mutants. EloA, Elongin A; VHL, VHL protein.

Fig. 7. Comparison of the amino acid sequences of rat and *C. elegans* Elongin A. Identical amino acids are shaded with black; chemically similar amino acids are shaded with gray. The Elongin BC binding site motif is boxed, and the region most highly conserved between rat and *C. elegans* Elongin A is underlined.

Fig. 8A. Analysis of wild type and mutant *C. elegans* Elongin A wherein wild type or mutant *C. elegans* Elongin A was refolded with rat Elongin B and C and subjected to TSK SP-NPR HPLC as described. Aliquots of the peak column fractions were analyzed by SDS-PAGE, and proteins were visualized by silver staining. WT C.e. EloA, wild type *C. elegans* Elongin A (SEQ ID NO:42); 202-434, *C. elegans* Elongin A mutant containing residues 202-434 (SEQ ID NO:45).

Fig. 8B. ~2 pmol of human or *C. elegans* Elongin A proteins were refolded as described (Bradslier et al. 1993a) in the presence or absence of ~2 pmol of rat Elongin B and C. Aliquots of refolded protein were assayed for transcriptional activity in oligo dc-tailed template assays performed as described. Reaction mixtures contained no Elongin (lane 1); 3 and 9 μl of renatured human Elongin A without (lanes 2 and 3) or with (lanes 4 and 5) Elongin B and C; 3 and 9 μl of renatured wild type *C. elegans* Elongin A without (lanes 6 and 7) or with (lanes 8 and 9) Elongin B and C; 3 and 9 μl of renatured C.e. EloA(94-434) (SEQ ID NO:44)

without (lanes 10 and 11) or with (lanes 12 and 13) Elongin B and C; 3 and 9 μl of renatured C.e. EloA (202-434) (SEQ ID NO:45) with (lanes 14 and 15) or without (lanes 16, and 17) Elongin B and C.

Fig. 9. Elongin C mutants analyzed in this study.

Fig. 10A. Assay of formation of Elongin BC complexes containing wild type and mutant Elongin C wherein wild type Elongin B (upper panel), wild type Elongin C (middle panel), or a mixture of wild type Elongin B and C were refolded and subjected to DEAE-NPR HPLC as described. Aliquots of the indicated column fractions were analyzed by SDS-PAGE, and proteins were visualized by silver staining.

Fig. 10B. N-terminal, C-terminal, and internal Elongin C deletion mutants were assayed for their abilities to form Elongin BC complexes as described.

Fig. 10C. Elongin C alanine scanning mutants were assayed for their abilities to form Elongin BC complexes as described. C(Ala19-21) (SEQ ID NO:61) co-electrophoreses with wild type Elongin B during SDS-PAGE. B, Elongin B; C, wild type or mutant Elongin C; L, load; FT, flow-through.

FIG. 11A. Assay of activation of Elongin A by wild type and mutant Elongin BC complexes wherein runoff transcription assays were performed as described according the protocol diagramed at the bottom of the figure. A mixture containing ~50 ng of SP-NPR purified Elongin A and ~5 ng (1x BC) or ~50 ng (10x BC) of purified wild type or mutant Elongin BC was preincubated on ice for 60 min prior to addition to

reaction mixtures. Purified Elongin BC complexes were from the following DEAE-NPR fractions shown in Fig. 10B: Wild type (SEQ ID NO:9), fraction 7; BC(15-112) (SEQ ID NO:46), fraction 5; BC(19-112) (SEQ ID NO:47), fraction 5; BC(1-97) (SEQ ID NO:51), fraction 6; and BC(1-83) (SEQ ID NO:52), fraction 5. Reactions shown in lanes 1 and 7 contained no Elongin BC. WT, wild type.

Fig. 11B. Runoff transcription assays were performed as described in the legend to Fig. 11A with Elongin BC complexes from the following DEAE-NPR fractions shown in Fig. 10B: wild type (SEQ ID NO:9), fraction 7, BC(Δ31-40) (SEQ ID NO:54), fraction 6; BC(Δ41-50) (SEQ ID NO:55), fraction 7; BC(Δ51-60) (SEQ ID NO:56), fraction 5; BC(Δ61-70) (SEQ ID NO:57), fraction 13; BC(Δ71-80) (SEQ ID NO:58), fraction 7; BC(Δ81-90) (SEQ ID NO:59), fraction 7; BC(Δ91-100) (SEQ ID NO:60), fraction 6. Runoff transcription is expressed in arbitrary units normalized to the amount of product synthesized in the presence of 1X (white boxes) or 10X (black boxes) wild type Elongin BC.

Fig. 12A. Assay of activation of Elongin A by Elongin C mutants that do not form isolable Elongin BC complexes. Runoff transcription assays were performed as described according to the protocol diagramed at the bottom of Fig. 11A. A mixture containing ~50 ng of SP-NPR purified Elongin A and ~5 ng (1xC) or ~50 ng (10xC) of Ni^{2+}-purified and refolded wild type or mutant Elongin C was preincubated on ice for 60 min and then added to reaction mixtures at -10°C.

Fig. 12B. Assay of activation of Elongin A by C(Ala19-21) (SEQ ID NO:61) and C(Ala22-24) (SEQ ID NO:62). Runoff transcription assays were performed as described in the legend to Fig. 11A with Elongin BC complexes from the following DEAE-NPR fractions shown in Fig. 10C: wild type BC, fraction 7; BC(Ala19-21) (SEQ ID NO:61), fraction 7; BC(Ala22-24) (SEQ ID NO:62), fraction 7. Runoff transcription is expressed in arbitrary units normalized to the amount of product synthesized in the presence of 1X (white boxes) or 10X (black boxes) wild type Elongin BC.

Fig. 13. Assay of formation of Elongin ABC complexes containing N-terminal and C-terminal Elongin C mutants. Mixtures containing wild type Elongin A and B and wild type or mutant Elongin C were refolded and subjected to SP-NPR HPLC as described. Aliquots of peak fractions from isolation of Elongin ABC complexes were analyzed by SDS-PAGE, and proteins were visualized by silver staining. A, Elongin A; B, Elongin B; C, wild type or mutant Elongin C.

Fig. 14A. Assay of formation and activity of Elongin ABC complexes containing Elongin C internal deletion mutants wherein formation of Elongin ABC complexes was assayed as described in the legend to Fig. 13.

Fig. 14B. Runoff transcription assays were performed as described according to the protocol diagramed at the bottom of Fig. 11A. Isolated Elongin ABC complexes were added to reactions at -10'. A, Elongin A; B, Elongin B; C, Elongin C.

Fig. 15. Assay of activation of Elongin A by isolated BC complexes containing Elongin C C-terminal alanine scanning mutants. Runoff transcription assays were performed as described in the legend to Fig. 11A. Runoff transcription is expressed in arbitrary units normalized to the amount of product synthesized in the presence of 1X (white boxes) or 10X (black boxes) wild type Elongin BC.

Fig. 16. Summary of Elongin C mutations that most strongly affect the ability of Elongin C to bind to Elongin B (B binding), to bind to Elongin A (A binding), and to activate Elongin A (Activation of Elongin A). Mutations in the region indicated by the open box strongly affect activation of Elongin A by isolated Elongin BC complexes but not of isolated Elongin ABC complexes. HZ, hydrophobic zipper.

DETAILED DESCRIPTION

The present invention relates to the Elongin A domains required for transcriptional elongation activation and for binding to Elongin BC and of the Elongin C domains required for interaction with Elongin B and activation of Elongin A's transcriptional elongation activity and the use of these domains.

Elongin A

Wild-type Elongin A is a 773 amino acid protein (SEQ ID NO:1) which stimulates the elongation activity of RNA Polymerase II. Fragments of the wild-type Elongin A having amino acid residues 1 to 730(SEQ ID NO:2), 1 to 680(SEQ ID NO:3), and 400-773(SEQ ID NO:4) each possess about 50% or more of the elongation activation activity exhibited by wild-type Elongin A. From the results it can be predicted that fragments of the wild-type Elongin A having amino acid residues 400-730 (SEQ ID NO:5) and 400-680 (SEQ ID NO:6) will also possess about 50% or more of the elongation activity exhibited by wild-type Elongin A.

The Elongin A sequence critical for binding to Elongins B and C also falls within this 374 amino acid sequence, i.e., between residues 400 and 773 (SEQ ID NO:4). This sequence, i.e., the Elongin B and C binding region of Elongin A, falls within a 20 amino acid region between residues 546 and 565 (SEQ ID NO:7) and preferably within a 12 amino acid region between residues 549 and 560 (SEQ ID NO:8).

Thus, the Elongin A region encompassing amino acid residues 400-773 (SEQ ID NO:4) includes all of the sequences necessary for full Elongin A transcriptional elongation activity and for regulation by Elongin BC. An Elongin A protein or fragment thereof containing this entire wild-type 374 amino acid region or a substantial portion of it will exhibit significant elongation activation activity and can be used in a variety of *in vitro* transcription systems or assays by one of ordinary skill in the art.

Elongin C

Wild-type Elongin C is a 112 amino acid protein (SEQ ID NO:9) which induces the transcriptional activity of Elongin A. The regions of the wild-type Elongin C required for (1) binding to Elongin B, (2) binding to Elongin A, and (3) activation of Elongin A transcriptional activity have now been localized. These regions are the amino acids between (1) residues 19 and 30 (SEQ ID NO:10), (2) residues 19 and 30 (SEQ ID NO:10) and 100 and 112 (SEQ ID NO:11), and (3) residues 19 and 30 (SEQ ID NO:10), 60 and 71 (SEQ ID NO:12)and 91-112 (SEQ ID NO:13), respectively.

Thus, an Elongin C protein or fragment thereof containing these wild-type regions will possess all sequences necessary for interaction and binding with Elongins A and B and can be used in a variety of *in vitro* transcription systems or assays by one of ordinary skill in the art.

Construction of the Elongin A and C subunits as well as N- and C- terminal and internal deletion mutants thereof was done as described in Examples 2 and 13. Expression and purification of these subunits was done as described in Examples 2, 3 and 14.

Identification and Characterization of the Elongin A Domains Required for Transcriptional Activation and Binding to Elongin BC

Elongin A is a 773 amino acid protein (SEQ ID NO:1) with a calculated molecular mass of 87.2 kDa as calculated from the amino acid sequence predicted from the cDNA. It has now been determined that an Elongin A region encompassing amino acids 400-773 (SEQ ID NO:4) includes all sequences necessary for full Elongin A transcriptional activity and for regulation by Elongin BC. The most critical sequences within the Elongin A transcriptional activation domain (residues 400-773) (SEQ ID NO:4) have been localized to an ~171 amino acid region between residues 520 and 690 (SEQ ID NO:14). Sequences outside this region, though not essential for activation of transcription, either participate in interactions with the RNA Polymerase II elongation complex or help to maintain the structural integrity of the transcriptional activation domain. Finally, the transcriptional activation domain of Elongin A has been found to be evolutionarily conserved in species as distantly related as *C. elongans* (nematode) and man.

It has also been determined that the Elongin A sequence critical for binding to Elongin B and C fall

within a 19 amino acid region between residues 546 and 565 (SEQ ID NO:7) and preferably within a 12 amino acid region between residues 549 and 560 (SEQ ID NO:8). This region shares a sequence similarity with a short region of the VHL protein (residues 157-172) (SEQ ID NO:15) previously shown to be sufficient for binding to Elongin B and C (Kibel, 1995). Within this conserved Elongin BC binding site motif (consensus sequence TLx3Cx2V[V,2]) SEQ ID NO:16 identical threonine, leucine, cysteine and valine are found in Elongin A and VHL at the positions designated 1, 2, 6 and 9 in SEQ ID NO:8 for Elongin A and in SEQ ID NO:15 for VHL protein.

Localization of the Elongin A Transcriptional Activation Domain

The Elongin A transcriptional activation domain was located and the Elongin BC binding site was identified using a series of N- and C-terminal Elongin A deletion mutants (Fig. 1A). These Elongin A deletion mutants were constructed, expressed in *E. coli*, purified, and assayed for their abilities (i) to assemble into chromatographically isolable Elongin ABC complexes and (ii) to stimulate the rate of elongation of transcripts synthesized by RNA Polymerase II from the AdML promoter in a reconstituted basal transcription system composed of TBP and the general initiation factors TFIIB, TFIIE, TFIIF, and TFIIH.

To test the abilities of Elongin A mutants to bind Elongin B and C and to isolate mutant Elongin ABC complexes for assay of their relative transcriptional

activities, N- and C-terminal Elongin A deletion mutants were refolded together with wild type Elongin B and C and subjected to TSK SP-NPR HPLC. Both wild type and mutant Elongin ABC complexes bind tightly to TSK SP-NPR and elute at salt concentrations between 0.2 and 0.4 M KCl, whereas excess Elongin B and C flow through this resin at 0.1 M KCl (Aso et al. 1995b). Fig. 1B shows SDS-PAGE analysis of aliquots of column fractions from TSK SP-NPR HPLC purification of wild type Elongin ABC complexes. Fig. 1C shows SDS-PAGE analysis of aliquots of peak column fractions from TSK SP-NPR HPLC purification of mutant Elongin ABC complexes: wild type (WT) (SEQ ID NO:1); 400-773 (SEQ ID NO:4); 1-730 (SEQ ID NO:2); 1-680 (SEQ ID NO:3); 1-630 (SEQ ID NO:17); and 1-535 (SEQ ID NO:18). Results of this analysis revealed that all N- and C-terminal Elongin A deletion mutants except A(1-535) (SEQ ID NO:18), which lacks the region similar to the Elongin BC binding site in the VHL protein (Kibel et al. 1995), were able to bind stably to Elongin B and C to form isolable Elongin ABC complexes.

The relative transcriptional activation activities of the wild type and mutant Elongin ABC complexes shown in Fig. 1C were then compared in runoff transcription assays. Preinitiation complexes were assembled at the AdML promoter, wild type and mutant Elongin ABC complexes were added to reaction mixtures, and transcription was initiated by addition of limiting concentrations of ribonucleoside triphosphates. Under these conditions, the rate of RNA chain elongation is

very slow, and runoff transcripts do not accumulate unless elongation stimulatory activity is present. Bradsher et al. 1993b; Aso et al. 1995b. Fig. 1D, lanes 1 and 2.

Results of these experiments indicated that the first 400 Elongin A amino acids (SEQ ID NO:19) (which include a region of SII similarity and a potential ATP binding site), are dispensable for Elongin ABC activity *in vitro*, since deletion of this region had no significant effect on accumulation of runoff transcripts. In contrast, deletion of the C terminal 93 amino acids (SEQ ID NO:3), which includes a potential hydrophobic zipper, decreased Elongin ABC activity by approximately 50%, and deletion of the C-terminal 143 amino acids (SEQ ID NO:17) abolished detectable Elongin ABC activity. Taken together, these results identified (i) a 20 amino acid Elongin A region (residues 546 to 565) (SEQ ID NO:7), which includes sequences required for interaction with Elongin B and C, (ii) a 281 amino acid Elongin A region (residues 400 to 680) (SEQ ID NO:6), which includes sequences required for transcriptional activity, and (iii) an additional C-terminal Elongin A region (residues 680 to 773) (SEQ ID NO:20), which includes sequences important for maximal transcriptional activity.

The Elongin A sequences required for binding to Elongin B and C and for transcriptional activity were further defined using a series of Elongin A internal deletion mutants. These mutants (Fig. 2A), with mutations spanning the transcriptional activation

domain from residues 400 to 730 (SEQ ID NO:5) were constructed, expressed in *E. coli*, purified, and assayed as described above. The mutant sequences tested were: Δ401-440 (SEQ ID NO:21); Δ441-480 (SEQ ID NO:22); Δ481-520 (SEQ ID NO:23); Δ521-545 (SEQ ID NO:24); Δ546-565 (SEQ ID NO:25); Δ566-585 (SEQ ID NO:26); Δ586-610 (SEQ ID NO:27); Δ611-650 (SEQ ID NO:28); Δ651-690 (SEQ ID NO:29); and Δ691-730 (SEQ ID NO:30).

All Elongin A internal deletion mutants, except Δ546-565 (SEQ ID NO:25), which lacks the region similar to the Elongin BC binding site found in the VHL protein (Kibel et al. 1995), were capable of binding to Elongin B and C (Figs. 2A and 2B). As shown in Fig. 2C, Elongin ABC complexes containing Elongin A internal deletion mutants Δ401-440 (SEQ ID NO:21), Δ441-480 (SEQ ID NO:22), Δ481-520 (SEQ ID NO:23), and Δ691-730 (SEQ ID NO:30) exhibited significant transcriptional activity. In contrast, Elongin ABC complexes containing Elongin A internal deletion mutants lacking sequences located in the region between amino acids 520 and 691 were profoundly impaired in their abilities to stimulate elongation by RNA Polymerase II.

Notably, the Elongin ABC complex containing Elongin A internal deletion mutant Δ521-545 (SEQ ID NO:24), which lacks a potential topoisomerase I catalytic site motif, is inactive in activating transcription. Topoisomerase I activity is unlikely to play a role in Elongin (SIII) function *in vitro*, however, because (i) we observed that mutating the

potential active site tyrosine at residue 543 to either phenylalanine or serine had no effect on Elongin A transcriptional activation activity (data not shown) and (ii) we have been unable to detect topoisomerase I activity associated with Elongin A

Taken together, analysis of the N-terminal, C-terminal, and internal Elongin A deletion mutants localized sequences critical for transcriptional activity to a minimal region of ~170 amino acids between residues 521 and 690 (SEQ ID NO:31). Further investigation revealed, however, that Elongin A sequences outside this minimal region also make significant contributions to the transcriptional activation activity of Elongin A. For example, Elongin A mutants composed of residues 500 to 730 (SEQ ID NO:32) or residues 500 to 700 (SEQ ID NO:33) were transcriptionally inactive, even though they assembled into isolable Elongin ABC complexes (Fig. 3). Thus, Elongin A sequences outside the minimal transcriptional activation domain make secondary contributions to Elongin activity, either by participating directly in interactions with the RNA Polymerase II elongation complex or by helping to maintain the proper three dimensional structure of the transcriptional activation domain.

Identification of the Elongin BC Binding Site

Analysis of Elongin A deletion mutants revealed that the Elongin A region between residues 546 and 565 (SEQ ID NO:7) plays an important role in binding to

Elongin B and C. As shown in Fig. 4A, this Elongin A region shares sequence similarity with a short region of the VHL protein (residues 157-172, underlined) (SEQ ID NO:15) previously shown to be sufficient for binding to Elongin B and C (Kibel et al. 1995). This Elongin A region was further defined using a systematic series of Elongin A internal deletion mutants spanning residues 545 to 568 (SEQ ID NO:34). These mutants (Fig. 4A) were constructed, expressed in *E. coli*, purified, and assayed for their abilities to assemble into chromatographically isolable Elongin ABC complexes and to stimulate the rate of elongation by RNA Polymerase II. The mutants tested were: Δ545-548 (SEQ ID NO:35); Δ549-552 (SEQ ID NO:36); Δ553-556 (SEQ ID NO:37); Δ557-560 (SEQ ID NO:38); Δ561-564 (SEQ ID NO:39); and Δ565-568 (SEQ ID NO:40).

As shown in Fig 4B, Elongin A internal deletion mutants Δ545-548 (SEQ ID NO:35), Δ561-564 (SEQ ID NO:39), and Δ565-568 (SEQ ID NO:40) bound stably to Elongin B and C to form Elongin ABC complexes that could be purified by TSK SP-NPR HPLC. In contrast, Elongin A internal deletion mutants Δ549-552 (SEQ ID NO:36), Δ553-556 (SEQ ID NO:37), and Δ557-560 (SEQ ID NO:38), each of which lack Elongin A sequences within the region most similar to the Elongin BC binding site of the VHL protein, were impaired in their abilities to bind to Elongin B and C.

To assess the transcriptional activities of the Elongin A internal deletion mutants, aliquots of peak fractions shown in Fig. 4B from TSK SP-NPR HPLC

purification of mutant Elongin ABC complexes were assayed for their abilities to stimulate the rate of elongation by RNA Polymerase II. Because they co-purified with variable amounts of Elongin B and C, these mutants were assayed in the absence (Fig. 5A) and presence (Fig. 5B) of excess purified Elongin BC complex.

The results of these assays revealed that all Elongin A deletion mutants with mutations between amino acid residues 545 and 568 were transcriptionally impaired, although not all mutants were impaired to the same extent. Two Elongin A deletion mutants, Δ545-548 (SEQ ID NO:35) and Δ565-568 (SEQ ID NO:40), which efficiently formed isolable Elongin ABC complexes, exhibited reduced but readily detectable transcriptional activity, whereas Elongin A mutant Δ561-564 (SEQ ID NO:39), which could also bind Elongin B and C, exhibited little activity. In addition, two Elongin A deletion mutants, Δ549-552 (SEQ ID NO:36) and Δ553-556 (SEQ ID NO:37), which were severely impaired in their abilities to form isolable Elongin ABC complexes, exhibited little or no detectable transcriptional activity, whereas Elongin A mutant Δ557-560 (SEQ ID NO:38), which was also impaired in its ability to form an isolable Elongin ABC complex, exhibited detectable activity, raising the possibility that deletion of Elongin A residues between 556 to 561 (SEQ ID NO:41) may result in an increase in the basal activity of Elongin A.

The results described above indicate that Elongin A sequences most critical for binding to Elongin B and C fall within a 12 amino acid region between residues 549 and 560 (SEQ ID NO:8). Both Elongin A (SEQ ID NO:8) and the VHL protein (SEQ ID NO:15) share conserved threonine, leucine, cysteine, and valine residues in their Elongin BC binding region at the positions designated 1, 2, 6, and 9 in Fig. 6. The importance of these residues is further underscored by investigations of mutations found in VHL families and in clear-cell renal carcinoma which have identified naturally occurring VHL point mutations of the conserved threonine, leucine, and cysteine residues, but not of the conserved valine residue (Latif et al. 1993; Gnarra et al. 1994; Chen et al. 1995; Kanno et al. 1994; Whaley et al. 1994; Foster et al. 1994).

To investigate the importance of these residues for Elongin A transcriptional activation activity, Elongin A mutants carrying point mutations of the conserved threonine, leucine, cysteine, and valine residues were constructed, expressed in *E. coli*, purified, and assayed for their abilities to form isolable Elongin ABC complexes and to stimulate the rate of elongation by RNA Polymerase II. As shown in Fig. 4B, each of the Elongin A point mutants, except L550S, formed readily detectable Elongin ABC complexes that could be purified by TSK SP-NPR HPLC, although Elongin A mutants T549I and C554F appeared somewhat impaired in their abilities to form Elongin ABC complexes.

To assess the transcriptional activities of the Elongin A point mutants, aliquots of peak fractions shown in Fig. 4B were assayed for their abilities to stimulate the rate of elongation by RNA Polymerase II in the absence (Fig. 5A) and presence (Fig. 5B) of excess purified Elongin BC complex. Only Elongin A point mutant V557E, which is mutated at a position where there are no corresponding naturally occurring VHL mutations, exhibited near wild type activity.

Evolutionary Conservation of the Elongin A Transcriptional Activation Domain

A TBLASTN search of the GenBank non-redundant database using rat Elongin A as the query sequence identified a predicted *C. elegans* ORF encoding a potential Elongin A homolog. By screening a *C. elegans* cDNA library with a probe derived from the predicted ORF, we isolated a cDNA encoding a highly basic, 434 amino acid protein (SEQ ID NO:42) with a calculated molecular mass of 49.2 kDa. Comparison of the predicted amino acid sequences of mammalian Elongin A and the potential *C. elegans* Elongin A homolog revealed two conserved regions: an N-terminal region resembling the SII-like N-terminus of mammalian Elongin A and a C-terminal region resembling the C-terminal transcriptional activation domain of mammalian Elongin A. Notably, the potential *C. elegans* Elongin A homolog exhibited the greatest similarity (33% identity, 53% similarity, alignment score 17.8 SD) to mammalian Elongin A residues 520 to 662 (SEQ ID NO:43), which

includes the majority of the region most critical for transcriptional activity (Fig. 7). In addition, this region of the *C. elegans* protein includes a short sequence that resembles the Elongin BC binding site found in the VHL protein; however, it lacks the topoisomerase I catalytic site motif.

To determine the functional relationship between mammalian Elongin A and the potential *C. elegans* Elongin A homolog, the intact *C. elegans* ORF and two N-terminal deletion mutants C.e.EloA(94-434) (SEQ ID NO:44) and C.e.EloA(202-434) (SEQ ID NO:45) were constructed, expressed in *E. coli*, purified, and assayed for their abilities to interact with mammalian Elongin B and C and to stimulate the rate of elongation by mammalian RNA Polymerase II. Mutant C.e.EloA(94-434) (SEQ ID NO:44) lacks sequences related to SII, but contains sequences similar to the Elongin A transcriptional activation and Elongin BC binding site. Mutant C.e.EloA contains the potential Elongin BC binding site, but lacks sequences similar to the N-terminus of the transcriptional activation domain of mammalian Elongin A.

Both the full-length C. elegans protein (SEQ ID NO:42) and mutants C.e.EloA(94-434) (SEQ ID NO:44) and C.e.EloA(202-434) (SEQ ID NO:45) were capable of binding to mammalian Elongin B and C (Fig. 8A and data not shown). In addition, the full-length *C. elegans* protein (SEQ ID NO:42) was capable of stimulating the rate of elongation by mammalian RNA Polymerase II in a reaction dependent on mammalian Elongin B and C (Fig.

8B). In these experiments, the transcriptional activities of mammalian Elongin A and the C. elegans protein were compared using an oligo(dC)-tailed template assay (Kadesch and Chamberlin, 1982; Tan et al. 1994a), which permits direct measurement of the effect of elongation factors on the rate of RNA chain elongation by RNA Polymerase II in the absence of initiation factors. Consistent with our results from analysis of mammalian Elongin A, mutant C.e.EloA(94-434)(SEQ ID NO:44), which contains the entire Elongin A-like transcriptional activation domain, was as active as the wild type C. elegans protein in stimulating the rate of elongation by mammalian RNA Polymerase II, whereas mutant C.e.EloA(202-434) (SEQ ID NO:45), which lacks the N-terminus of the Elongin A-like transcriptional activation domain, had significantly reduced activity.

Identification and Characterization of the Elongin C Domains Required for Interaction with Elongin B and Activation of Elongin A

Elongin C is a 112 amino acid protein (SEQ ID NO:9) with a calculated mass of 12.4 kD as calculated from the amino acid sequence predicted from the cDNA. Elongin C is a regulatory subunit of the Elongin ABC which (i) functions as a potent stimulator of Elongin A transcriptional activation activity, (ii) interacts specifically with Elongin B to form an isolable Elongin BC complex, and (iii) is bound and negatively regulated *in vitro* by the product of the von Hippel-Lindau (VHL) tumor suppressor gene. As described herein, the

Elongin C regions important for binding to Elongin B and for binding to and activating of Elongin A have now been localized.

Identification of an Elongin C Region Important for Binding to Elongin B

The regions of Elongin C which interact with Elongin B were localized using a systematic series of N-terminal, C-terminal, and internal Elongin C deletion mutants. These mutants (Fig. 9) were constructed, expressed in E. coli, purified, and assayed for their abilities to form chromatographically isolable Elongin BC complexes. The mutants tested were: 15-112 (SEQ ID NO:46); 19-112 (SEQ ID NO:47); 23-112 (SEQ ID NO:48); 29-112 (SEQ ID NO:49); 57-112 (SEQ ID NO:50); 1-97 (SEQ ID NO:51); 1-83 (SEQ ID NO:52); Δ21-30 (SEQ ID NO:53); Δ31-40 (SEQ ID NO:54); Δ41-50 (SEQ ID NO:55); Δ51-60 (SEQ ID NO:56); Δ61-70 (SEQ ID NO:57); Δ71-80 (SEQ ID NO:58); Δ81-90 (SEQ ID NO:59); Δ91-100 (SEQ ID NO:60); Ala19-21 (SEQ ID NO:61); Ala22-24 (SEQ ID NO:62); Ala25-27 (SEQ ID NO:63); Ala28-30 (SEQ ID NO:64); Ala89-91 (SEQ ID NO:65); Ala92-94 (SEQ ID NO:66); Ala95-97 (SEQ ID NO:67); Ala98-100 (SEQ ID NO:68); Ala101-103 (SEQ ID NO:69); Ala104-106 (SEQ ID NO:70); Ala107-109 (SEQ ID NO:71); and Ala110-112 (SEQ ID NO:72).

In these experiments, individual Elongin C mutants were refolded together with wild type Elongin B and subjected to TSK DEAE-NPR HPLC. The Elongin BC complex elutes from TSK DEAE-NPR as a discrete species with

chromatographic properties distinct from those of both wild type Elongin B, which flows through TSK DEAE-NPR at low ionic strength, and wild type Elongin C, which binds tighter to this resin than the Elongin BC complex (Fig 10A). As shown in Fig. 10B, deletion of as many as 29 amino acids from the C-terminus of Elongin C (SEQ ID NO:52) had no detectable effect on formation of isolable Elongin BC complexes. Likewise, deletion of as many as 18 amino acids from the N-terminus of Elongin C (SEQ ID NO:47) had no detectable effect on formation of isolable Elongin BC complexes.

Deletion of 22 amino acids (SEQ ID NO:48) from the N-terminus of Elongin C, however, abolished formation of isolable Elongin BC complexes. This suggests that Elongin C residues between 18 and 22 (SEQ ID NO:73) are critical for interaction of Elongin B and C. Consistent with this possibility, an Elongin C internal deletion mutant lacking residues 21 to 30 (SEQ ID NO:53) did not form an isolable Elongin BC complex (Fig. 10B). Notably, this mutant was the only Elongin C internal deletion mutant that failed to bind to Elongin B, suggesting that the Elongin C region between residues 18 and 30 (SEQ ID NO:74) either contains the Elongin B binding site or is crucial for proper folding of the protein.

Further evidence supporting the importance of Elongin C sequences within this region, i.e., residues 18 to 30 (SEQ ID NO:74), for binding to Elongin B came from analysis of a set of clustered alanine scanning mutants in which Elongin C residues between amino acids

19 and 30 (SEQ ID NO:10) were mutated three at a time to alanines. As shown in Fig. 10C, although Elongin C alanine scanning mutants C(Ala19-21) (SEQ ID NO:61) and C(Ala22-24) (SEQ ID NO:62) were capable of assembling into isolable Elongin BC complexes, C(Ala25-27) (SEQ ID NO:63) and C(Ala28-30) (SEQ ID NO:64) were not.

Characterization of Elongin C Regions Important for Activation of Elongin A

Pre-assembled Elongin BC complexes are capable of activating Elongin A. To investigate the requirements for activation of Elongin A by Elongin C, the isolated wild type and mutant Elongin BC complexes shown in Fig. 10A and Fig. 10B were assayed for their abilities to stimulate the rate of accumulation of runoff transcripts synthesized by RNA Polymerase II from the AdML promoter in a reconstituted transcription system containing purified Elongin A and the general initiation factors TBP, TFIIB, TFIIE, TFIIF, and TFIIH. As shown in Figs. 11A and 11B, the entire C-terminal half of Elongin C is critical for activation of Elongin A by pre-assembled Elongin BC complexes. Elongin BC complexes containing Elongin C deletion mutants lacking up to 18 amino acids from their N-termini (SEQ ID NO:46; SEQ ID NO:47) or sequences between amino acids 41 and 60 (SEQ ID NO:55; SEQ ID NO:56) were capable of activating Elongin A. Elongin BC complexes containing Elongin C deletion mutants lacking as few as 15 amino acids from their C-terminal (SEQ ID NO:51) were inactive. (Fig. 11A) Furthermore, Elongin BC

complexes containing Elongin C internal deletion mutants lacking sequences C-terminal to amino acid 61 (SEQ ID NO:57; SEQ ID NO:58; SEQ ID NO:59; SEQ ID NO:60) were inactive, and an Elongin BC complex containing the internal deletion mutant CΔ31-40 (SEQ ID NO:54), which lacks sequences immediately C-terminal to the region important for Elongin B binding, was also inactive.

Although Elongin B facilitates assembly and enhances stability of the Elongin ABC complex, it is not essential for activation of Elongin A by Elongin C. As described above, Elongin C mutants containing mutations in the region between amino acids 19 and 30 (SEQ ID NO:10) were unable to form isolable Elongin BC complexes. To investigate the ability of these Elongin C mutants to activate Elongin A, they were assayed for their abilities to stimulate the rate of accumulation of runoff transcripts synthesized by RNA Polymerase II from the AdML promoter in the presence of Elongin A and the general initiation factors, but in the absence of Elongin B. As shown in Fig. 12A, although wild type Elongin C strongly activated Elongin A, none of the Elongin C mutants containing mutations between amino acids 19 and 30 (SEQ ID NO:10), except alanine scanning mutant C(Ala22-24) (SEQ ID NO:62) (Fig. 12B), was capable of activating Elongin A. Thus, the Elongin C region between amino acids 19 and 30 (SEQ ID NO:10) is important for both Elongin B binding and activation of Elongin A.

To investigate whether Elongin C deletion mutants that fail to activate Elongin A are defective in their abilities to bind Elongin A, the Elongin C deletion mutants were assayed for their abilities to form chromatographically isolable Elongin ABC complexes. In these experiments, individual Elongin C deletion mutants were refolded together with wild type Elongin A and B and subjected to TSK SP-NPR HPLC. As described previously, Elongin A, Elongin AC and Elongin ABC complexes bind tightly to TSK SP-NPR and can all be eluted with ~0.3 M KCl, whereas Elongin B and C flow through this resin at low ionic strength.

As shown in Fig. 13, the N-terminal Elongin C deletion mutant C(15-112) (SEQ ID NO:46) and C(19-112) (SEQ ID NO:47), which form isolable Elongin BC complexes that activate Elongin A, were capable of assembling into isolable Elongin ABC complexes, whereas the remaining N-terminal and C-terminal Elongin C deletion mutants (C(23-112) (SEQ ID NO:48); C(29-112) (SEQ ID NO:49); C(57-112) (SEQ ID NO:50); C(1-97) (SEQ ID NO:51); and C(1-83) (SEQ ID NO:52)), each of which form inactive Elongin BC complexes, were unable to form isolable Elongin ABC complexes.

In contrast, with the exception of Elongin C internal deletion mutant, C(Δ21-30) (SEQ ID NO:53), which lacks residues 21 to 30 and does not form an isolable Elongin BC complex, each of the Elongin C internal deletion mutants (C(Δ31-40) (SEQ ID NO:54); C(Δ41-50) (SEQ ID NO:55); C(Δ51-60) (SEQ ID NO:56); C(Δ61-70) (SEQ ID NO:57); C(Δ71-80) (SEQ ID NO:58);

C(Δ81-90) (SEQ ID NO:59); C(Δ91-100) (SEQ ID NO:60)) was capable of forming an isolable Elongin ABC complex (Fig. 14A). In these experiments, the yield of Elongin B and C in purified Elongin ABC complexes containing Elongin C internal deletion mutants was routinely less than their yield in purified Elongin ABC complexes containing wild type Elongin C, suggesting that Elongin ABC complexes containing the internal deletion mutants assemble less efficiently or are less stable than wild type Elongin ABC complexes.

Runoff transcription assays were used to compare the activities of the isolated wild type and mutant Elongin ABC complexes shown in Fig. 14A. The concentration of the wild type Elongin ABC complex in the reaction shown in lane 2 of Fig. 14B was sufficient to saturate the assay, and the concentrations of mutant Elongin ABC complexes were adjusted so that all reactions shown in Fig. 14B contained equivalent levels of Elongin A. Results of transcription assays highlighted the importance of sequences at the C-terminus of Elongin C for activation of Elongin A. Elongin ABC complexes containing Elongin C mutants Δ91-100 (SEQ ID NO:60), Δ61-70 (SEQ ID NO:57), and Δ21-30 (SEQ ID NO:53) were unable to stimulate the rate of elongation by RNA Polymerase II.

In addition, although Elongin BC complexes containing Elongin C internal deletion mutants C(Δ71-80) (SEQ ID NO:58) and C(Δ81-90) (SEQ ID NO:59) were unable to activate Elongin A, Elongin ABC complexes containing these same Elongin C mutants were capable of

stimulating the rate of elongation by RNA Polymerase II, suggesting that the Elongin C region between amino acids 71 and 90 is not critical for activation of Elongin A in Elongin ABC complexes assembled by folding all three subunits together.

It is noteworthy that the activity of mutant Elongin ABC complexes does not, in all cases, correlate with the amount of Elongin B and C present. Elongin ABC complexes containing Elongin C internal deletion mutant C(Δ71-80) (SEQ ID NO:58) are considerably more active than those containing C(Δ81-90) (SEQ ID NO:59), even though Elongin ABC complexes containing C(Δ81-90) (SEQ ID NO:59) contain more Elongin B and C. Thus, the results of these experiments demonstrate that binding of Elongin C to Elongin A is not sufficient for activation of Elongin A, and they indicate the importance of the C-terminus of Elongin C for activation of Elongin A.

Further evidence supporting the importance of the C-terminus of Elongin C in activation of Elongin A came from an analysis of a set of clustered alanine scanning mutants in which Elongin C residues between 89 and 112 (SEQ ID NO:75) were mutated three at a time to alanines. As predicted, all C-terminal alanine scanning mutants were capable of binding to Elongin B to form chromatographically isolable Elongin BC complexes (data not shown). In addition, although Elongin BC complexes containing three of these mutants, C(Ala89-91) (SEQ ID NO:65), C(Ala98-100) (SEQ ID NO:68), and C(Ala107-109) (SEQ ID NO:71), were nearly

as active as wild type BC complexes, the activity of BC complexes containing C(Ala92-94) (SEQ ID NO:66), C(Ala95-97) (SEQ ID NO:67), C(Ala101-103) (SEQ ID NO:69), C(Ala104-106) (SEQ ID NO:70), and C(Ala110-112) (SEQ ID NO:72) was significantly impaired (Fig. 15).

Elongin C mutations fall into several classes based on their effects on Elongin C activities (Fig. 16). First, the only Elongin C mutations that had dramatic effects on Elongin B binding fell within a short Elongin C region between amino acids 19 and 30 (SEQ ID NO:10). This is consistent with the possibility that sequences within this region are directly involved in interactions with Elongin B. Deletion mutations in this region, however, were also found to affect the ability of Elongin C to assemble into isolable Elongin ABC complexes and to activate Elongin A transcriptional activity. Thus, it is also possible that some mutations in this region disrupt the overall tertiary structure of Elongin C.

Second, the only Elongin C mutations that had dramatic effects on formation of isolable Elongin ABC complexes without affecting formation of Elongin BC complexes were mutations in the extreme C-terminus of Elongin C. This result, together with our finding that all Elongin C internal deletion mutants (C(Δ31-40) (SEQ ID NO:54); C(Δ41-50) (SEQ ID NO:55); (CΔ51-60) (SEQ ID NO:56); C(Δ61-70) (SEQ ID NO:57); C(Δ71-80) (SEQ ID NO:58); C(Δ81-90) (SEQ ID NO:59); and C(Δ91-100) (SEQ ID NO:60), except C(Δ21-30) (SEQ ID NO:53), were capable of forming isolable Elongin ABC complexes,

suggests that the C-terminus of Elongin C plays a crucial role in binding Elongin A.

Third, Elongin C mutations that affect formation of Elongin ABC complexes are only a subset of those mutations that affect the elongation activation activity of Elongin A, indicating that binding of Elongin C by Elongin A is not sufficient for activation of Elongin A. Interestingly, the size of the Elongin C region sensitive to mutations that affect activation of Elongin A was dependent on the assay used to measure activation. In one assay, which measured the ability of Elongin C or Elongin BC complexes to stimulate the rate of elongation by RNA Polymerase II in the presence of Elongin A, Elongin C mutations that fell within the entire C-terminal half of the protein (residues 61-112) (SEQ ID NO:76) drastically reduced Elongin C activity. In contrast, in a second assay, which measured the ability of preassembled Elongin ABC complexes to stimulate the rate of elongation by RNA Polymerase II, Elongin C mutations that fell between residues 71 and 90 had a significantly reduced effect on Elongin A activity, indicating that sequences within this Elongin C region are not essential for activation of Elongin A.

Examples

Identification of Elongin A Domains

Example 1 - Materials

Unlabeled ultrapure ribonucleoside 5'-triphosphates were purchased from Pharmacia Biotech Inc. [α-^{32}P]CTP (>400 Ci/mmol) was obtained from

Amersham Corp. Phenylmethylsulfonyl fluoride (PMSF), heparin, and polyvinyl alcohol type II were from Sigma Chemical Co. (St. Louis, Mo). Bovine serum albumin (Pentex fraction V) was purchased from ICN ImmunoBiologicals. Glycerol (Spectranlyzed grade) and guanidine hydrochloride (electrophoresis grade) were obtained from Fisher Scientific.

Example 2 - Expression and purification of wild type and mutant rat Elongin A

Overexpression of rat Elongin A mutants in E. coli was accomplished using an M13mpET bacteriophage expression system (Garrett et al. 1994; Garrett et al. 1995). Constructs for expression of 6-histidine-tagged N- and C-terminal Elongin A deletion mutants, were prepared by inserting PCR generated fragments of the Elongin A cDNA into the Sal I and Bam HI sites of M13mpET. Constructs for expression of Elongin A internal deletion and point mutants were prepared by oligonucleotide-directed mutagenesis (Kunkel, 1985) using the Muta-Gene M13 *in vitro* mutagenesis kit (Bio-Rad). Elongin A mutants were sequenced by the dideoxy chain-termination method using a Sequenase kit (United States Biochemicals).

To prepare Elongin A mutants, 500 ml cultures of *E. coli* strain JM109(DE3) was grown to an OD_{600} of 0.6 in Luria broth containing 2.5 mM $MgCl_2$ at 37°C with gentle shaking. Cells were infected with M13mpET vectors carrying mutant Elongin A cDNAs at a multiplicity of infection of 20. After an additional 2

hours at 37°C, cells were induced with 0.4 mM isopropyl β-D-thiogalactoside, and cultures were incubated for an additional 2.5 hours. Cells were harvested by centrifugation at 2000 x g for 10 min at 4°C. The cell pellets were resuspended in 25 ml of ice-cold 20 mM Tris-HCl (pH 8.0), 10 mM imidazole (pH 8.0), and 1 mg/ml lysozyme and incubated on ice for 30 min. After 2 cycles of freeze-thaw, the suspension was centrifuged at 100,000 x g for 35 min at 4°C. Inclusion bodies were solubilized by resuspension in 25 ml of ice-cold 50 mM Tris-HCl (pH 8.0) containing 6 M guanidine hydrochloride, and the resulting suspension was clarified by centrifugation at 50,000 x g for 20 min at 4°C. Recombinant Elongin A mutants were purified from the supernatant by Ni^{2+} -nitrilotriacetic acid-agarose (Invitrogen) affinity chromatography as described (Garrett et al. 1994; Aso et al. 1995b).

Example 3 - Reconstitution and purification of Elongin complexes containing Elongin A mutants

Recombinant Elongin B and C were expressed in *E. coli* using the M13mpET bacteriophage expression system and purified as described previously (Garrett et al. 1994; Garrett et al. 1995). Reconstitution of Elongin complexes was carried out essentially as described (Aso et al. 1995b) by refolding ~50 μg of wild type or mutant Elongin A, ~8 μg of Elongin B, and ~8 μg of Elongin C. Following dialysis, the mixtures were centrifuged at 60,000 x g for 15 min at 4°C. The resulting supernatant were applied to TSK SP-NPR

columns (35 mm x 4.6 mm, Hewlett-Packard) equilibrated in 40 mM Hepes-NaOH (pH 7.9), 0.1 mM EDTA, 1 mM DTT, 10% (v/v) glycerol; and 0.1 M KCl and fractionated using a SMART microchromatography system (Pharmacia) at 8°C. The columns were eluted at 0.6 ml/min with a 9 ml linear gradient from 0.1 to 0.8 M KCl in the same buffer. Aliquots of each column fraction were analyzed by 12% SDS-polyacrylainide gel electrophoresis (PAGE), and the proteins were visualized by silver staining.

Example 4 - Preparation of RNA Polymerase II and initiation factors

RNA Polymerase II (Conaway and Conaway, 1990) and TFIIH (rat δ, TSK DEAE 5-PW fraction) (Conaway et al. 1992) were purified as described from rat liver nuclear extracts. Recombinant yeast TBP (Conaway et al. 1991) and rat TFIIB (rat α) (Tsuboi et al. 1992) were expressed in *E. coli* and purified as described. Recombinant TFIIE was prepared as described (Peterson et al. 1991), except that the 56 kDa subunit was expressed in BL21(DE3)-pLysS. Recombinant TFIIF was purified as described (Tan et al. 1994b) from *E. coli* strain JM109(DE3) infected with M13mpET-RAP30 and M13mpET-RAP74.

Example 5 - Runoff transcription assays

Unless indicated otherwise, preinitiation complexes were assembled as described (Garrett et al. 1995) by preincubation of 50 ng of the EcoRl to Ndel fragment from pDN-AdML (Conaway and Conaway, 1988) and

approximately 10 ng of recombinant TFIIB, 10 ng of recombinant TFIIF, 7 ng of recombinant TFIIE, 40 ng of TFIIH (rat δ, fraction VI), 50 ng of recombinant yeast TBP (AcA 44 fraction), and 0.01 units of RNA Polymerase II. Transcription was initiated by addition of 7 mM $MgCl_2$, 50 μM ATP, 2 μM UTP, 10 μM CTP, 50 μM GTP, and 10 μCi [α-^{32}P]CTP, either in the presence or absence of Elongin preparations. After incubation at 28°C for the times indicated in the legends, runoff transcripts were analysed by electrophoresis through 6% polyacrylamide, 7.0 M urea gels. Transcription was quantitated using a Molecular Dynamics phosphorimager.

Example 6 - Oligo(dC)-tailed template assay of elongation by RNA Polymerase II

Pulse-chase assays were carried out essentially as described (Aso et al. 1995b). 0.01 unit of RNA Polymerase III and 100 ng of pCpGR220S/P/X were incubated at 28°C in the presence of 20 mM Hepes-NaOH, pH 7.9, 20 mM Tris-HCl, pH 7.9, 2% (w/v) polyvinyl alcohol, 0.5 mg/ml bovine serum albumin, 60 mM KCl, 50 μM ZnSO4, 7 mM $MgCl_2$, 0.2 mM dithiothreitol, 3% (v/v) glycerol, 3 units of recombinant RNAsin (Promega), 50 μM ATP, 50 μM GTP, 2 μM CTP, and 10 μCi of [α-^{32}P]CTP. After 25 min of labeling, the reactions were chased for 7.5 min following addition of 100 μM non-radioactive CTP, 2 μM UTP, and the indicated amounts of Elongin preparations. Transcripts were analysed by electrophoresis through 6% polyacrylamide, 7.0 M urea gels.

Example 7 - Isolation of CDNA encoding *C. elegans* Elongin A

A homology search of the GeneBank database using rat Elongin A protein sequence as the query revealed that nucleotides 19335 through 21154 of *C. elegans* cosmid R03D7 contained a predicted ORF encoding a protein highly homologous to portions of Elongin A. A λ ZAP *C. elegans* cDNA library was constructed and screened with the 5'-^{32}P-labeled oligonucleotide 5'-GAG TTG GTC AGT GCT CGC GTG GTC AAG AAC AGG CTT CAG TAG ATC AAA TGG-3' (SEQ ID NO:77), which corresponds to a portion of the predicted ORF. Hybridization was performed at 65°C for 20 hours in 5x standard saline citrate, 5x Denhardt's solution, 100 mM sodium phosphate, 0.1% sodium dodecyl sulfate, 10% dextran sulfate containing denatured salmon testis DNA (100 μg/ml). Three overlapping cDNA clones with inserts of up to 1.8 kb were isolated. Clone CE22, which contained the longest insert, was sequenced on both strands by the dideoxy chaintermination method using a Sequenase kit (United States Biochemicals).

Example 8 - Expression and purification of C elegans Elongin A

Histidine-tagged *C. elegans* Elongin A was overexpressed in *E. coli* using a pET16b expression vector (Novagen). The pET16b constructs for expression of histidine-tagged wild type and mutant *C. elegans* Elongin A were prepared by insertion of PCR-generated fragments of the *C. elegans* ORF into the Nde I and Bam HI sites of the pET16b vector. A 100 ml culture of *E.*

coli strain BL21(DE3) transformed with pET16b carrying the *C. elegans* Elongin A cDNA was grown to an OD_{600} of 0.6 in Luria broth containing 50 μg/ml ampicillin at 37°C. Following induction with 1 mM isopropyl β-D-thiogalactoside, the culture was incubated for an additional 2.5 hours at 37°C. Cells were harvested by centrifugation at 2000 x g for 10 min at 4°C. The cell pellet was resuspended in 5 ml of ice-cold 20 mM Tris-HCl (pH 8.0), 10 mM imidazole (pH 8.0), and 1 mg/ml lysozyme and incubated on ice for 30 min. After 2 cycles of freeze-thaw, the suspension was centrifuged at 100,000 x g for 35 min at 4°C. Inclusion bodies were solubilized by resuspension in 5 ml of ice-cold 50 mM Tris-HCl (pH 8.0) containing 6 M guanidine hydrochloride, and the resulting suspension was clarified by centrifugation at 50,000 x g for 20 min at 4°C. Recombinant wild type and mutant *C. elegans* Elongin A were purified from the supernatant by Ni^{2+}-nitrilotriacetic acid-agarose (Invitrogen) affinity chromatography as described (Garrett et al. 1994).

Identification of Elongin C Domains

Example 9 - Materials

Unlabeled ultrapure ribonucleoside 5'-triphosphates were purchased from Pharmacia Biotech Inc. Restriction enzymes were obtained from American Allied Biochemicals or Promega. [α-^{32}P]CTP (> 650 Ci/mmol) was from Amersham Corp. Proteinase K and isopropyl β-D-thiogalactoside (IPTG) were purchased from Sigma Chemical Co. Bovine serum albumin (Pentex

fraction V, reagent grade) was obtained from ICN Immunobiologicals. Guanidine hydrochloride (Sequanal grade) was obtained from Pierce Chemical Co. Phenylmethylsulfonyl fluoride (PMSF) was from Sigma Chemical Co. and was dissolved in dimethylsulfoxide to 1 M. Polyvinyl alcohol (average molecular weight 30,000-70,000) was from Sigma Chemical Co. and was dissolved in water to 20% (w/v) and centrifuged or filtered through a 0.2 μ filter prior to use.

Example 10 - DNA template for transcription

pDN-AdML (19) plasmid DNA was isolated from *E. coli* using the Triton-lysozyme method (20). Plasmid DNA was banded twice in CsCl-ethidium bromide density gradients, precipitated with ethanol, and dissolved in TE buffer (20 mM Tris-HCl, pH 7.6, 1 mM EDTA). A restriction fragment prepared by digestion of pDN-AdML DNA with EcoRI and NdeI was used as the template in transcription reactions. The fragment was purified from a 1.0% low melting temperature agarose gel using GELase (Epicentre Technologies) according to the manufacturer's instructions. After phenol-chloroform extraction and ethanol precipitation, purified DNA fragments were resuspended in TE buffer.

Example 11 - Preparation of RNA Polymerase II and transcription factors

RNA Polymerase II (21) and TFIIH (rat δ, TSK DEAE 5-PW fraction) (22) were purified as described from rat liver nuclear extracts. Recombinant yeast TBP (23) and

rat TFIIB (rat δ) (24) were expressed in *E. coli* and purified as described. Recombinant TFIIE was prepared as described (25), except that the 56-kDa subunit was expressed in BL21(DE3)-pLysS. Recombinant TFIIF was purified as described (26) from *E. coli* strain JM109(DE3) infected with M13mpET-RAP30 and M13mpET-RAP74.

Example 12 - Runoff transcription assays

All reaction mixtures were 60 μl. Preinitiation complexes were assembled by preincubation of approximately 10 ng template DNA (EcoRI to NdeI fragment from pDN-AdML), ~10 ng of recombinant TFIIB, ~10 ng of recombinant TFIIF, ~7 ng of recombinant TFIIE, ~40 ng of rat TFIIH, ~20 ng of TBP, ~0.01 unit of RNA Polymerase II, and ~8 units of RNAsin in 20 mM Hepes-NaOH (pH 7.9), 20 mM Tris-HCl (pH 7.9), 60 mM KCl, 2 mM DTT, 0.5 mg/ml bovine serum albumin, 2% (w/v) polyvinyl alcohol, and 3% (v/v) glycerol for 30 min at 28°C. Elongin, Elongin subassemblies, or Elongin subunits were then added to reaction mixtures in the amounts and at the times indicated in the figure legends. Transcription was initiated by addition of 7 mM $MgCl_2$ and 50 μM ATP, 50 μM GTP, 10 μM CTP, 2 μM UTP and 10 μCi [α-^{32}P]CTP. After incubation of reaction mixtures for 9 min at 28°C, runoff transcripts were analyzed by electrophoresis through 6% polyacrylamide gels containing 7.0 M urea. Transcription was quantitated using a Molecular Dynamics phosphorimager.

Example 13 - Construction of Elongin C mutants

Elongin C mutants were constructed by oligonucleotide-directed mutagenesis (27) of M13mpET-Elongin C (16) with the Muta-Gene M13 *in vitro* mutagenesis kit (Bio-Rad) and confirmed by dideoxy DNA sequencing with the *fmol* DNA Sequencing System (Promega). Mutagenic oligonucleotides included 15 nucleotides from the parental rat Elongin C sequence (16) on either side of the deletion point. Mutagenic oligonucleotides for alanine scanning mutagenesis included 12 nucleotides from the parental rat Elongin C on either side of the alanine substitution point.

Example 14 - Expression and purification of Elongin subunits

Histidine-tagged Elongin A was overexpressed in *E. coli* using a pET16b expression vector (Novagen). The pET16b-Elongin A construct for expression of histidine-tagged Elongin A was prepared by insertion of a PCR-generated fragment containing the entire rat Elongin A open reading frame (18) into the NdeI and BamHI sites of the pET-16b vector. A 1L culture of *E. coli* strain BL21(DE3) transformed with pET16b-Elongin A was grown to an OD_{600} of 0.6 in Luria broth (LB) (20) containing 100 μg/ml carbenicillin at 37°C. Following induction with 0.5 mM IPTG, the culture was incubated for an additional 3 hours at 37°C. Cells were harvested by centrifugation at 2000 X g for 10 min at 4°C. The cell pellet was resuspended in 50 ml of ice-cold 20 mM Tris-HCl (pH 8.0), 10 mM imidazole (pH 8.0), and 1 mg/ml

lysozyme and incubated on ice for 30 min. After 2 cycles of freeze-thaw, the suspension was centrifuged at 100,000 X g for 35 min. Inclusion bodies were solubilized by resuspension in 50 ml of ice-cold 6 M guanidine hydrochloride, 40 mM Tris-HCl(pH 8.0), 10 mM imidazole (pH 8.0), 0.5 mM PMSF, and 0.5 M KCl, and the resulting suspension was clarified by centrifugation at 100,000 X g for 35 min.

Recombinant Elongin A was purified from the supernatants by Ni^{2+}-nitrilotriacetic acid-agarose (Invitrogen) affinity chromatography. Ni^{2+} chromatography was performed at 4°C. 10 ml of supernatant was applied to a 2 ml Ni^{2+}-column pre-equilibrated with 6 M guanidine hydrochloride, 20 mM Tris-HCl(pH 7.9), 10 mM imidazole (pH 8.0), 0.5 M KCl, and 0.5 mM PMSF. The column was washed with 10 ml of 5.7 M guanidine hydrochloride, 40 mM Tris-HCl (pH 7.9), 40 mM imidazole (pH 8.0), and 0.5 mM PMSF, and recombinant Elongin A was eluted with 4.2 M guanidine hydrochloride, 40 mM Tris-HCl (pH 7.9), 300 mM imidazole (pH 8.0), and 0.5 mM PMSF.

Overexpression of Elongin B and wild type and mutant Elongin C was accomplished using the M13mpET bacteriophage expression system (16,17). A 100 ml culture of *E. coli* strain JM109(DE3) (Promega) was grown to an OD_{600} of 0.6 in Luria broth at 37°C. Cells were infected with M13pET bacteriophage carrying the wild type rat Elongin B or wild type or mutant rat Elongin C cDNAs at a multiplicity of infection of 10-20. After an additional 2 hours at 37°C, cells were

induced with 0.5 mM IPTG, and cultures were incubated an additional 3 hours. Cells were harvested by centrifugation at 2000 X g for 10 min at 4°C. The cell pellet was resuspended in 7 ml of 20 mM Tris-HCl (pH 8.0), 10 mM imidazole (pH 8.0), and 1 mg/ml lysozyme and incubated on ice for 30 min. After 2 cycles of freeze-thaw, the suspension was centrifuged at 100,000 X g for 35 min. Inclusion bodies were solubilized by resuspension in 7 ml of ice-cold 6 M guanidine hydrochloride, 40 mM TrisHCl (pH 8.0), 10 mM imidazole (pH 8.0), 0.5 mM PMSF, and 0.5 M KCl, and the resulting suspension was clarified by centrifugation at 100,000 X g for 35 min. Wild type Elongin B and wild type and mutant Elongin C were purified using Ni^{2+}-column chromatography as described above.

Example 15 - Assay of Elongin BC complex formation

~6 μg of Elongin B was mixed with ~6 μg of either wild type or mutant Elongin C and diluted 5 fold with 40 mM Hepes-NaOH (pH 7.9), 100 mM KCl, 2 mM DTT, 50 μM $ZnSO_4$, 0.1 mM EDTA, and 10% (v/v) glycerol. After incubation for 90 min on ice, the mixtures were dialyzed at 4°C overnight against 40 mM Tris-HCl (pH 7.9), 0.1 mM EDTA, 10% (v/v) glycerol, and 40 mM KCl. Following dialysis, the mixtures were centrifuged at 60,000 X g for 15 min at 4°C. The resulting supernatants were applied to TSK DEAE-NPR columns (35 mm X 4.6 mm, Toso-Haas) pre-equilibrated in 40 mM Tris-HCl (pH 7.9), 0.1 mM EDTA, 1 mM DTT, 10% (v/v) glycerol, and 40 mM KCl and fractionated using a SMART

microchromatography system (Pharmacia) at 8°C. The columns were eluted at 0.3 ml/min with a 3 ml linear gradient from 0.04 to 0.5 M KCl in 40 mM Tris-HCl (pH 7.9), 0.1 mM EDTA, 1 mM DTT, and 10% (v/v) glycerol. Aliquots of each column fraction were analyzed by 10% Tris-Tricine SDS-polyacrylamide gel electrophoresis (28), and the proteins were visualized by silver staining.

Example 16 - Assay of Elongin ABC complex formation

~45 μg of Elongin A, ~6 μg of Elongin B, and ~6 μg of either wild type or mutant Elongin C were diluted 5 fold with 40 mM Hepes-NaOH (pH 7.9), 100 mM KCl, 50 μm $ZnSO_4$, and 10% (v/v) glycerol. After incubation for 90 min on ice, the mixtures were dialyzed at 4°C overnight against 40 mM Tris-HCl (pH 7.9), 0.1 mM EDTA, 10% (v/v) glycerol, and 40 mM KCl. Following dialysis, the mixtures were centrifuged at 60,000 X g for 15. min at 4°C. The resulting supernatants were applied to TSK SP-NPR columns (35 mm X 4.6 mm, Toso-Haas) pre-equilibrated in 40 mM Hepes-NaOH (pH 7.9), 1 mM DTT, 10% (v/v) glycerol, and 0.1 M KCl and fractionated using a SMART microchromatography system (Pharmacia) at 8°C. The columns were eluted at 0.6 ml/min with a 9 ml linear gradient from 0.1 to 0.8 M KCl in 40 mM Hepes-NaOH (pH 7.9), 1 mM DTT, and 10% (v/v) glycerol. Aliquots of each column fraction were analyzed by 10% Tris-Tricine SDS-polyacrylamide gel electrophoresis (28), and the proteins were visualized by silver staining.

SEQUENCE LISTING

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(I) TELEX: N/A

(ii) TITLE OF INVENTION: ELONGIN A AND C FUNCTIONAL DOMAINS

(iii) NUMBER OF SEQUENCES: 77

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(F) ZIP: 75270-2197

(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30

(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:

(viii) ATTORNEY/AGENT INFORMATION:
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(B) REGISTRATION NUMBER: 31,966
(C) REFERENCE/DOCKET NUMBER: 11146/07502

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(B) TELEFAX: 214-981-3400

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 773 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..773
(D) OTHER INFORMATION: /note= "entire amino acid sequence of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

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195 200 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
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245 250 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
260 265 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
275 280 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
290 295 300

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            660                 665                 670

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        675                 680                 685

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(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 730 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..730
(D) OTHER INFORMATION: /note= "amino acids 1-730 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

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        195                 200                 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

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225                 230                 235                 240

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                245                 250                 255

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Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285

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    290                 295                 300

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        515                 520                 525

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            580                 585                 590

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        595                 600                 605

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    610                 615                 620

Trp Arg Glu Met Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu
625                 630                 635                 640

Arg Leu Leu Thr Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys
                645                 650                 655

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            660                 665                 670

Arg Asp Val Arg Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala
        675                 680                 685
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Val Pro Glu Lys Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser
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(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 680 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..680
(D) OTHER INFORMATION: /note= "amino acids 1-680 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

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        35                  40                  45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
    50                  55                  60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65                  70                  75                  80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
                85                  90                  95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
            100                 105                 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
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Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
180 185 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
195 200 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
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His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225 230 235 240

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245 250 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
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Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
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Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
325 330 335

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Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
355 360 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
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Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
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420 425 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
435 440 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
450 455 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465 470 475 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro
485 490 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
500 505 510

Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg
515 520 525

Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
530 535 540

Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn
545 550 555 560

Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu
565 570 575

Glu Pro Val Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu
580 585 590

Glu Cys Asn His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val
595 600 605

His Cys His Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser
610 615 620

Trp Arg Glu Met Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu
625 630 635 640

Arg Leu Leu Thr Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys
645 650 655

Gly Arg Gln Ala Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro
660 665 670

Arg Asp Val Arg Arg Arg Gln Glu
675 680

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 374 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..374
(D) OTHER INFORMATION: /note= "amino acids 400-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Thr Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys
1 5 10 15

Lys Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly
20 25 30

```
Leu Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala
        35                  40                  45

Gln Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro
    50                  55                  60

Ala Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu
65                  70                  75                  80

Pro Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg
                85                  90                  95

Pro Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys
            100                 105                 110

Ala Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg
        115                 120                 125

Arg Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr
    130                 135                 140

Leu Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys
145                 150                 155                 160

Asn Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val
                165                 170                 175

Leu Glu Pro Val Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile
            180                 185                 190

Glu Glu Cys Asn His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys
        195                 200                 205

Val His Cys His Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu
    210                 215                 220

Ser Trp Arg Glu Met Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg
225                 230                 235                 240

Leu Arg Leu Leu Thr Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro
                245                 250                 255

Lys Gly Arg Gln Ala Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro
            260                 265                 270

Pro Arg Asp Val Arg Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala
        275                 280                 285

Ala Val Pro Glu Lys Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly
    290                 295                 300

Ser Ser His Val Pro Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser
305                 310                 315                 320

Pro Glu Glu Leu Ala Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu
                325                 330                 335

Ala Pro Val Ala Ser Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala
            340                 345                 350
```

Val Lys Lys Ile Ala Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys
355 360 365

Asn Arg Phe Ser Arg Arg
370

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 331 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..331
(D) OTHER INFORMATION: /note= "amino acids 400-730 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

Thr Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys
1 5 10 15

Lys Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly
20 25 30

Leu Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala
35 40 45

Gln Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro
50 55 60

Ala Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu
65 70 75 80

Pro Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg
85 90 95

Pro Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys
100 105 110

Ala Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg
115 120 125

Arg Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr
130 135 140

Leu Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys
145 150 155 160

Asn Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val
165 170 175

Leu Glu Pro Val Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile
180 185 190

```
Glu Glu Cys Asn His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys
        195                 200                 205

Val His Cys His Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu
    210                 215                 220

Ser Trp Arg Glu Met Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg
225                 230                 235                 240

Leu Arg Leu Leu Thr Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro
                245                 250                 255

Lys Gly Arg Gln Ala Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro
            260                 265                 270

Pro Arg Asp Val Arg Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala
        275                 280                 285

Ala Val Pro Glu Lys Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly
    290                 295                 300

Ser Ser His Val Pro Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser
305                 310                 315                 320

Pro Glu Glu Leu Ala Tyr Glu Gly Pro Ser Thr
                325                 330
```

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 281 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..281
(D) OTHER INFORMATION: /note= "amino acids 400-680 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

```
Thr Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys
1               5                   10                  15

Lys Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly
            20                  25                  30

Leu Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala
        35                  40                  45

Gln Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro
    50                  55                  60

Ala Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu
65                  70                  75                  80
```

```
Pro Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg
                85                  90                  95

Pro Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys
            100                 105                 110

Ala Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg
        115                 120                 125

Arg Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr
    130                 135                 140

Leu Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys
145                 150                 155                 160

Asn Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val
                165                 170                 175

Leu Glu Pro Val Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile
            180                 185                 190

Glu Glu Cys Asn His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys
        195                 200                 205

Val His Cys His Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu
    210                 215                 220

Ser Trp Arg Glu Met Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg
225                 230                 235                 240

Leu Arg Leu Leu Thr Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro
                245                 250                 255

Lys Gly Arg Gln Ala Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro
            260                 265                 270

Pro Arg Asp Val Arg Arg Arg Gln Glu
        275                 280
```

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "amino acids 546-565 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

```
Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn Asn
1               5                  10                  15
```

Ile Asp Ser Ile
20

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..12
(D) OTHER INFORMATION: /note= "amino acids 549-560 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn
1 5 10

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 112 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..112
(D) OTHER INFORMATION: /note= "entire amino acid sequence of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
50 55 60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65 70 75 80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
85 90 95

Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys
100 105 110

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..12
(D) OTHER INFORMATION: /note= "amino acids 19-30 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile
1 5 10

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 13 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..13
(D) OTHER INFORMATION: /note= "amino acids 100-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys
1 5 10

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..12
(D) OTHER INFORMATION: /note= "amino acids 60-71 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Val Asn Phe Arg Glu Ile Pro Ser His Val Leu Ser
1 5 10

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..22
(D) OTHER INFORMATION: /note= "amino acids 91-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala
1 5 10 15

Ala Asn Phe Leu Asp Cys
20

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 171 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..171
(D) OTHER INFORMATION: /note= "amino acids 520-690 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Glu Glu Ala Gly Phe Thr Gly Arg Arg Met Asn Ser Lys Met Gln Val
1 5 10 15

Tyr Ser Gly Ser Lys Cys Ala Tyr Leu Pro Lys Met Met Thr Leu His
20 25 30

```
Gln Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser Ile Phe Glu
        35                  40                  45

Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu Glu Arg Cys
    50                  55                  60

Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His Val Leu Ile
65                  70                  75                  80

Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg Asp Phe Lys
                85                  90                  95

Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met Tyr Leu Arg
            100                 105                 110

Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr Asn Asn Ile
        115                 120                 125

Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met Ala
    130                 135                 140

Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg Arg Arg Gln
145                 150                 155                 160

Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro
                165                 170
```

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..16
(D) OTHER INFORMATION: /note= "amino acids 157-172 of VHL protein"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

```
Thr Leu Lys Glu Arg Cys Leu Gln Val Val Arg Ser Leu Val Lys Pro
1               5                   10                  15
```

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..12
(D) OTHER INFORMATION: /note= "consensus sequence"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

Thr Leu Xaa Xaa Xaa Cys Xaa Xaa Val Xaa Xaa Xaa
1 5 10

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 630 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..630
(D) OTHER INFORMATION: /note= "amino acids 1-630 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1 5 10 15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
20 25 30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
35 40 45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
50 55 60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65 70 75 80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
85 90 95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
100 105 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
115 120 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
130 135 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145 150 155 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
165 170 175

```
Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
            180                 185                 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
        195                 200                 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225                 230                 235                 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
                245                 250                 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
            260                 265                 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
    290                 295                 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305                 310                 315                 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
                325                 330                 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
            340                 345                 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
        355                 360                 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
    370                 375                 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385                 390                 395                 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
                405                 410                 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
            420                 425                 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
        435                 440                 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
    450                 455                 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465                 470                 475                 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro
                485                 490                 495
```

```
Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
            500                 505                 510

Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg
        515                 520                 525

Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
    530                 535                 540

Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn
545                 550                 555                 560

Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu
                565                 570                 575

Glu Pro Val Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu
            580                 585                 590

Glu Cys Asn His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val
        595                 600                 605

His Cys His Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser
    610                 615                 620

Trp Arg Glu Met Tyr Leu
625                 630
```

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 535 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..535
(D) OTHER INFORMATION: /note= "amino acids 1-535 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

```
Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1               5                   10                  15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
            20                  25                  30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
        35                  40                  45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
    50                  55                  60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65                  70                  75                  80
```

```
Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
                85                  90                  95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
            100                 105                 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
        115                 120                 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
    130                 135                 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145                 150                 155                 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
                165                 170                 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
            180                 185                 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
        195                 200                 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225                 230                 235                 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
                245                 250                 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
            260                 265                 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
    290                 295                 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305                 310                 315                 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
                325                 330                 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
            340                 345                 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
        355                 360                 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
    370                 375                 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385                 390                 395                 400
```

```
Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
                405                 410                 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
            420                 425                 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
        435                 440                 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
    450                 455                 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465                 470                 475                 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro
                485                 490                 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
            500                 505                 510

Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg
        515                 520                 525

Met Asn Ser Lys Met Gln Val
    530                 535
```

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 400 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..400
(D) OTHER INFORMATION: /note= "amino acids 1-400 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

```
Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1               5                   10                  15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
            20                  25                  30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
        35                  40                  45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
    50                  55                  60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65                  70                  75                  80
```

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
85 90 95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
100 105 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
115 120 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
130 135 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145 150 155 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
165 170 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
180 185 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
195 200 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
210 215 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225 230 235 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
245 250 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
260 265 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
275 280 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
290 295 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305 310 315 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
325 330 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
340 345 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
355 360 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
370 375 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385 390 395 400

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 94 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..94
(D) OTHER INFORMATION: /note= "amino acids 680-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys Val Arg Ile
1 5 10 15

Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn
20 25 30

Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly
35 40 45

Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val
50 55 60

Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met
65 70 75 80

Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg
85 90

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 733 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..733
(D) OTHER INFORMATION: /note= "amino acids 1-400 and 441-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1 5 10 15

```
Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
            20                  25                  30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
        35                  40                  45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
    50                  55                  60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65                  70                  75                  80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
                85                  90                  95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
            100                 105                 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
        115                 120                 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
    130                 135                 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145                 150                 155                 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
                165                 170                 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
            180                 185                 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
        195                 200                 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225                 230                 235                 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
                245                 250                 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
            260                 265                 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
    290                 295                 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305                 310                 315                 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
                325                 330                 335
```

```
Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
            340                 345                 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
        355                 360                 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
    370                 375                 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385                 390                 395                 400

Ser Lys Asn Leu Asn Ser Ala Gln Lys Leu Pro Lys Ala Asn Glu Asn
                405                 410                 415

Lys Ser Asp Lys Leu Gln Pro Ala Gly Ala Glu Pro Thr Arg Pro Arg
            420                 425                 430

Lys Val Pro Thr Asp Val Leu Pro Ala Leu Pro Asp Ile Pro Leu Pro
        435                 440                 445

Ala Ile Gln Thr Asn Tyr Arg Pro Leu Pro Ser Leu Glu Leu Ile Ser
    450                 455                 460

Ser Phe Gln Pro Lys Arg Lys Ala Phe Ser Ser Pro Gln Glu Glu Glu
465                 470                 475                 480

Glu Ala Gly Phe Thr Gly Arg Arg Met Asn Ser Lys Met Gln Val Tyr
                485                 490                 495

Ser Gly Ser Lys Cys Ala Tyr Leu Pro Lys Met Met Thr Leu His Gln
            500                 505                 510

Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser Ile Phe Glu Val
        515                 520                 525

Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu Glu Arg Cys Thr
    530                 535                 540

Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His Val Leu Ile Glu
545                 550                 555                 560

Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg Asp Phe Lys Glu
                565                 570                 575

Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met Tyr Leu Arg Leu
            580                 585                 590

Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr Asn Asn Ile Arg
        595                 600                 605

Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met Ala Phe
    610                 615                 620

Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg Arg Arg Gln Glu
625                 630                 635                 640

Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys Val Arg Ile Lys
                645                 650                 655
```

```
Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn Ser
            660                 665                 670

Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly Pro
        675                 680                 685

Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val Ser
    690                 695                 700

Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met Ala
705                 710                 715                 720

Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg
                725                 730
```

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 733 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..733
(D) OTHER INFORMATION: /note= "amino acids 1-440 and 481-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

```
Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1               5                   10                  15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
            20                  25                  30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
        35                  40                  45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
    50                  55                  60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65                  70                  75                  80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
                85                  90                  95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
            100                 105                 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
        115                 120                 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
    130                 135                 140
```

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145 150 155 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
165 170 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
180 185 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
195 200 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
210 215 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225 230 235 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
245 250 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
260 265 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
275 280 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
290 295 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305 310 315 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
325 330 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
340 345 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
355 360 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
370 375 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385 390 395 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
405 410 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
420 425 430

Lys Lys Lys Asp Ser Lys Ser Thr Ala Leu Pro Asp Ile Pro Leu Pro
435 440 445

Ala Ile Gln Thr Asn Tyr Arg Pro Leu Pro Ser Leu Glu Leu Ile Ser
450 455 460

```
Ser Phe Gln Pro Lys Arg Lys Ala Phe Ser Ser Pro Gln Glu Glu Glu
465                 470                 475                 480

Glu Ala Gly Phe Thr Gly Arg Arg Met Asn Ser Lys Met Gln Val Tyr
                485                 490                 495

Ser Gly Ser Lys Cys Ala Tyr Leu Pro Lys Met Met Thr Leu His Gln
            500                 505                 510

Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser Ile Phe Glu Val
        515                 520                 525

Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu Glu Arg Cys Thr
    530                 535                 540

Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His Val Leu Ile Glu
545                 550                 555                 560

Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg Asp Phe Lys Glu
                565                 570                 575

Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met Tyr Leu Arg Leu
            580                 585                 590

Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr Asn Asn Ile Arg
        595                 600                 605

Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met Ala Phe
    610                 615                 620

Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg Arg Arg Gln Glu
625                 630                 635                 640

Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys Val Arg Ile Lys
                645                 650                 655

Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn Ser
            660                 665                 670

Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly Pro
        675                 680                 685

Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val Ser
    690                 695                 700

Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met Ala
705                 710                 715                 720

Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg
                725                 730
```

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 733 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..733
(D) OTHER INFORMATION: /note= "amino acids 1-480 and 521-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

```
Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1               5                  10                  15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
            20                  25                  30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
        35                  40                  45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
    50                  55                  60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65                  70                  75                  80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
                85                  90                  95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
            100                 105                 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
        115                 120                 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
    130                 135                 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145                 150                 155                 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
                165                 170                 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
            180                 185                 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
        195                 200                 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225                 230                 235                 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
                245                 250                 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
            260                 265                 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285
```

```
Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
290                 295                 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305                 310                 315                 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
                325                 330                 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
            340                 345                 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
        355                 360                 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
    370                 375                 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385                 390                 395                 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
                405                 410                 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
            420                 425                 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
        435                 440                 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
    450                 455                 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465                 470                 475                 480

Glu Ala Gly Phe Thr Gly Arg Arg Met Asn Ser Lys Met Gln Val Tyr
                485                 490                 495

Ser Gly Ser Lys Cys Ala Tyr Leu Pro Lys Met Met Thr Leu His Gln
            500                 505                 510

Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser Ile Phe Glu Val
        515                 520                 525

Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu Glu Arg Cys Thr
    530                 535                 540

Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His Val Leu Ile Glu
545                 550                 555                 560

Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg Asp Phe Lys Glu
                565                 570                 575

Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met Tyr Leu Arg Leu
            580                 585                 590

Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr Asn Asn Ile Arg
        595                 600                 605
```

```
Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met Ala Phe
    610                 615                 620

Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg Arg Arg Gln Glu
625                 630                 635                 640

Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys Val Arg Ile Lys
                645                 650                 655

Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn Ser
            660                 665                 670

Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly Pro
        675                 680                 685

Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val Ser
    690                 695                 700

Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met Ala
705                 710                 715                 720

Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg
                725                 730
```

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 748 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..748
(D) OTHER INFORMATION: /note= "amino acids 1-520 and 546-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

```
Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1               5                   10                  15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
            20                  25                  30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
        35                  40                  45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
    50                  55                  60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65                  70                  75                  80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
                85                  90                  95
```

```
Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
            100                 105                 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
        115                 120                 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
    130                 135                 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145                 150                 155                 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
                165                 170                 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
            180                 185                 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
        195                 200                 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225                 230                 235                 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
                245                 250                 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
            260                 265                 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
    290                 295                 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305                 310                 315                 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
                325                 330                 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
            340                 345                 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
        355                 360                 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
    370                 375                 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385                 390                 395                 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
                405                 410                 415
```

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
420 425 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
435 440 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
450 455 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465 470 475 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro
485 490 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
500 505 510

Phe Ser Ser Pro Gln Glu Glu Glu Lys Met Met Thr Leu His Gln Gln
515 520 525

Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser Ile Phe Glu Val Gly
530 535 540

Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu Glu Arg Cys Thr Pro
545 550 555 560

Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His Val Leu Ile Glu Glu
565 570 575

Thr Asp Gln Leu Trp Lys Val His Cys His Arg Asp Phe Lys Glu Glu
580 585 590

Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met Tyr Leu Arg Leu Gln
595 600 605

Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr Asn Asn Ile Arg Ser
610 615 620

Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met Ala Phe Val
625 630 635 640

Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg Arg Arg Gln Glu Lys
645 650 655

Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys Val Arg Ile Lys Pro
660 665 670

Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn Ser Ser
675 680 685

Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly Pro Ser
690 695 700

Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val Ser Tyr
705 710 715 720

Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met Ala Lys
725 730 735

Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg
740 745

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 753 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..753
(D) OTHER INFORMATION: /note= "amino acids 1-545 and 566-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1 5 10 15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
20 25 30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
35 40 45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
50 55 60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65 70 75 80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
85 90 95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
100 105 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
115 120 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
130 135 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145 150 155 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
165 170 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
180 185 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
195 200 205

```
Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225                 230                 235                 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
                245                 250                 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
            260                 265                 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
    290                 295                 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305                 310                 315                 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
                325                 330                 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
            340                 345                 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
        355                 360                 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
    370                 375                 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385                 390                 395                 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
                405                 410                 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
            420                 425                 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
        435                 440                 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
    450                 455                 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465                 470                 475                 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro
                485                 490                 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
            500                 505                 510

Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg
        515                 520                 525
```

```
Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
    530                 535                 540

Pro Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu
545                 550                 555                 560

Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His
                565                 570                 575

Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg
            580                 585                 590

Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met
        595                 600                 605

Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr
    610                 615                 620

Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala
625                 630                 635                 640

Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg
                645                 650                 655

Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys
            660                 665                 670

Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro
        675                 680                 685

Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala
    690                 695                 700

Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser
705                 710                 715                 720

Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala
                725                 730                 735

Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg
            740                 745                 750

Arg
```

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 753 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..753
(D) OTHER INFORMATION: /note= "amino acids 1-565 and 586-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

```
Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1               5                  10                  15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
            20                  25                  30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
        35                  40                  45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
    50                  55                  60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65                  70                  75                  80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
                85                  90                  95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
            100                 105                 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
        115                 120                 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
    130                 135                 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145                 150                 155                 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
                165                 170                 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
            180                 185                 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
        195                 200                 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225                 230                 235                 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
                245                 250                 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
            260                 265                 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
    290                 295                 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305                 310                 315                 320
```

```
Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
                325                 330                 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
            340                 345                 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
        355                 360                 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
    370                 375                 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385                 390                 395                 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
                405                 410                 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
            420                 425                 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
        435                 440                 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
    450                 455                 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465                 470                 475                 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro
                485                 490                 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
            500                 505                 510

Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg
        515                 520                 525

Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
    530                 535                 540

Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn
545                 550                 555                 560

Asn Ile Asp Ser Ile Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His
                565                 570                 575

Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg
            580                 585                 590

Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met
        595                 600                 605

Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr
    610                 615                 620

Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala
625                 630                 635                 640
```

```
Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg
                645                 650                 655

Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys
            660                 665                 670

Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro
        675                 680                 685

Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala
    690                 695                 700

Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser
705                 710                 715                 720

Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala
                725                 730                 735

Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg
            740                 745                 750

Arg
```

(2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 748 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..748
(D) OTHER INFORMATION: /note= "amino acids 1-585 and 611-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

```
Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1               5                   10                  15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
            20                  25                  30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
        35                  40                  45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
    50                  55                  60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65                  70                  75                  80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
                85                  90                  95
```

```
Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
            100                 105                 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
        115                 120                 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
    130                 135                 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145                 150                 155                 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
                165                 170                 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
            180                 185                 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
        195                 200                 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225                 230                 235                 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
                245                 250                 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
            260                 265                 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
    290                 295                 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305                 310                 315                 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
                325                 330                 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
            340                 345                 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
        355                 360                 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
    370                 375                 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385                 390                 395                 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
                405                 410                 415
```

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
420 425 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
435 440 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
450 455 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465 470 475 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro
485 490 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
500 505 510

Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg
515 520 525

Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
530 535 540

Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn
545 550 555 560

Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu
565 570 575

Glu Pro Val Leu Glu Arg Cys Thr Pro His Arg Asp Phe Lys Glu Glu
580 585 590

Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met Tyr Leu Arg Leu Gln
595 600 605

Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr Asn Asn Ile Arg Ser
610 615 620

Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met Ala Phe Val
625 630 635 640

Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg Arg Arg Gln Glu Lys
645 650 655

Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys Val Arg Ile Lys Pro
660 665 670

Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn Ser Ser
675 680 685

Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly Pro Ser
690 695 700

Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val Ser Tyr
705 710 715 720

Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met Ala Lys
725 730 735

Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg
740 745

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 733 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: nct relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..733
(D) OTHER INFORMATION: /note= "amino acids 1-610 and 651-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1 5 10 15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
20 25 30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
35 40 45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
50 55 60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65 70 75 80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
85 90 95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
100 105 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
115 120 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
130 135 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145 150 155 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
165 170 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
180 185 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
195 200 205

```
Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225                 230                 235                 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
                245                 250                 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
            260                 265                 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
    290                 295                 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305                 310                 315                 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
                325                 330                 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
            340                 345                 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
        355                 360                 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
    370                 375                 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385                 390                 395                 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
                405                 410                 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
            420                 425                 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
        435                 440                 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
    450                 455                 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465                 470                 475                 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro
                485                 490                 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
            500                 505                 510

Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg
        515                 520                 525
```

```
Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
    530                 535                 540

Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn
545                 550                 555                 560

Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu
                565                 570                 575

Glu Pro Val Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu
            580                 585                 590

Glu Cys Asn His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val
        595                 600                 605

His Cys His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met Ala Phe
    610                 615                 620

Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg Arg Arg Gln Glu
625                 630                 635                 640

Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys Val Arg Ile Lys
                645                 650                 655

Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn Ser
            660                 665                 670

Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly Pro
        675                 680                 685

Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val Ser
    690                 695                 700

Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met Ala
705                 710                 715                 720

Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg
                725                 730
```

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 733 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..733
(D) OTHER INFORMATION: /note= "amino acids 1-650 and 691-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

```
Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1               5                   10                  15
```

```
Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
            20                  25                  30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
        35                  40                  45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
    50                  55                  60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65                  70                  75                  80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
                85                  90                  95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
            100                 105                 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
        115                 120                 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
    130                 135                 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145                 150                 155                 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
                165                 170                 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
            180                 185                 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
        195                 200                 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225                 230                 235                 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
                245                 250                 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
            260                 265                 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
    290                 295                 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305                 310                 315                 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
                325                 330                 335
```

```
Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
            340                 345                 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
        355                 360                 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
    370                 375                 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385                 390                 395                 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
                405                 410                 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
            420                 425                 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
        435                 440                 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
    450                 455                 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465                 470                 475                 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro
                485                 490                 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
            500                 505                 510

Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg
        515                 520                 525

Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
    530                 535                 540

Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn
545                 550                 555                 560

Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu
                565                 570                 575

Glu Pro Val Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu
            580                 585                 590

Glu Cys Asn His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val
        595                 600                 605

His Cys His Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser
    610                 615                 620

Trp Arg Glu Met Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu
625                 630                 635                 640

Arg Leu Leu Thr Asn Asn Ile Arg Ser Ala Glu Lys Val Arg Ile Lys
                645                 650                 655
```

```
Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn Ser
            660                 665                 670

Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly Pro
        675                 680                 685

Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val Ser
    690                 695                 700

Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met Ala
705                 710                 715                 720

Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg
                725                 730
```

(2) INFORMATION FOR SEQ ID NO:30:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 733 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..733
(D) OTHER INFORMATION: /note= "amino acids 1-690 and 731-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

```
Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1               5                   10                  15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
            20                  25                  30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
        35                  40                  45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
    50                  55                  60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65                  70                  75                  80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
                85                  90                  95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
            100                 105                 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
        115                 120                 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
    130                 135                 140
```

```
Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145                 150                 155                 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
                165                 170                 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
            180                 185                 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
        195                 200                 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225                 230                 235                 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
                245                 250                 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
            260                 265                 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
    290                 295                 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305                 310                 315                 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
                325                 330                 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
            340                 345                 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
        355                 360                 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
    370                 375                 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385                 390                 395                 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
                405                 410                 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
            420                 425                 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
        435                 440                 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
    450                 455                 460
```

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

```
Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala Phe Ser Ser
1               5                  10                  15

Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg Met Asn Ser
            20                  25                  30

Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu Pro Lys Met
        35                  40                  45

Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp
    50                  55                  60

Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val
65                  70                  75                  80

Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn
                85                  90                  95

His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His
            100                 105                 110

Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu
        115                 120                 125

Met Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu
    130                 135                 140

Thr Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln
145                 150                 155                 160

Ala Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val
                165                 170                 175

Arg Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu
            180                 185                 190

Lys Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val
        195                 200                 205

Pro Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu
    210                 215                 220

Ala Tyr Glu Gly Pro Ser Thr
225                 230
```

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 201 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..201

(D) OTHER INFORMATION: /note= "amino acids 500-700 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala Phe Ser Ser
1 5 10 15

Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg Met Asn Ser
20 25 30

Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu Pro Lys Met
35 40 45

Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp
50 55 60

Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val
65 70 75 80

Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn
85 90 95

His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His
100 105 110

Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu
115 120 125

Met Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu
130 135 140

Thr Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln
145 150 155 160

Ala Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val
165 170 175

Arg Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu
180 185 190

Lys Val Arg Ile Lys Pro Ala Pro Tyr
195 200

(2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..24
(D) OTHER INFORMATION: /note= "amino acids 545-568 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn
1 5 10 15

Asn Ile Asp Ser Ile Phe Glu Val
20

(2) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 769 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..769
(D) OTHER INFORMATION: /note= "amino acids 1-544 and 549-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1 5 10 15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
20 25 30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
35 40 45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
50 55 60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65 70 75 80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
85 90 95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
100 105 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
115 120 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
130 135 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145 150 155 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
165 170 175

```
Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
            180                 185                 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
        195                 200                 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225                 230                 235                 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
                245                 250                 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
            260                 265                 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
    290                 295                 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305                 310                 315                 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
                325                 330                 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
            340                 345                 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
        355                 360                 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
    370                 375                 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385                 390                 395                 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
                405                 410                 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
            420                 425                 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
        435                 440                 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
    450                 455                 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465                 470                 475                 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro
                485                 490                 495
```

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
500 505 510

Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg
515 520 525

Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
530 535 540

Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser
545 550 555 560

Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu
565 570 575

Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His
580 585 590

Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg
595 600 605

Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met
610 615 620

Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr
625 630 635 640

Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala
645 650 655

Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg
660 665 670

Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys
675 680 685

Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro
690 695 700

Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala
705 710 715 720

Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser
725 730 735

Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala
740 745 750

Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg
755 760 765

Arg

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 769 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..769
(D) OTHER INFORMATION: /note= "amino acids 1-548 and 553-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

```
Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1               5                  10                  15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
            20                  25                  30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
        35                  40                  45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
    50                  55                  60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65                  70                  75                  80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
                85                  90                  95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
            100                 105                 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
        115                 120                 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
    130                 135                 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145                 150                 155                 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
                165                 170                 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
            180                 185                 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
        195                 200                 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225                 230                 235                 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
                245                 250                 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
            260                 265                 270
```

```
Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
    290                 295                 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305                 310                 315                 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
                325                 330                 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
            340                 345                 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
        355                 360                 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
    370                 375                 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385                 390                 395                 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
                405                 410                 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
            420                 425                 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
        435                 440                 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
    450                 455                 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465                 470                 475                 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro
                485                 490                 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
            500                 505                 510

Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg
        515                 520                 525

Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
    530                 535                 540

Pro Lys Met Met Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser
545                 550                 555                 560

Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu
                565                 570                 575

Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His
            580                 585                 590
```

Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg
595 600 605

Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met
610 615 620

Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr
625 630 635 640

Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala
645 650 655

Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg
660 665 670

Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys
675 680 685

Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro
690 695 700

Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala
705 710 715 720

Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser
725 730 735

Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala
740 745 750

Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg
755 760 765

Arg

(2) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 769 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..769
(D) OTHER INFORMATION: /note= "amino acids 1-552 and 557-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1 5 10 15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
20 25 30

```
Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
        35                  40                  45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
    50                  55                  60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65                  70                  75                  80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
                85                  90                  95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
            100                 105                 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
        115                 120                 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
    130                 135                 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145                 150                 155                 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
                165                 170                 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
            180                 185                 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
        195                 200                 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225                 230                 235                 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
                245                 250                 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
            260                 265                 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
    290                 295                 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305                 310                 315                 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
                325                 330                 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
            340                 345                 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
        355                 360                 365
```

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
370 375 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385 390 395 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
405 410 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
420 425 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
435 440 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
450 455 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465 470 475 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro
485 490 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
500 505 510

Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg
515 520 525

Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
530 535 540

Pro Lys Met Met Thr Leu His Gln Val Leu Lys Asn Asn Ile Asp Ser
545 550 555 560

Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu
565 570 575

Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His
580 585 590

Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg
595 600 605

Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met
610 615 620

Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr
625 630 635 640

Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala
645 650 655

Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg
660 665 670

Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys
675 680 685

Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro
690 695 700

Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala
705 710 715 720

Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser
725 730 735

Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala
740 745 750

Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg
755 760 765

Arg

(2) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 769 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..769
(D) OTHER INFORMATION: /note= "amino acid 1-556 and 561-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1 5 10 15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
20 25 30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
35 40 45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
50 55 60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65 70 75 80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
85 90 95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
100 105 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
115 120 125

```
Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
    130                 135                 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145                 150                 155                 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
                165                 170                 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
            180                 185                 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
        195                 200                 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225                 230                 235                 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
                245                 250                 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
            260                 265                 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
        275                 280                 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
    290                 295                 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305                 310                 315                 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
                325                 330                 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
            340                 345                 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
        355                 360                 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
    370                 375                 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385                 390                 395                 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
                405                 410                 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
            420                 425                 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
        435                 440                 445
```

```
Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
    450                 455                 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465                 470                 475                 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro
                485                 490                 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
            500                 505                 510

Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg
        515                 520                 525

Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
    530                 535                 540

Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Asn Ile Asp Ser
545                 550                 555                 560

Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu
                565                 570                 575

Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His
            580                 585                 590

Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg
        595                 600                 605

Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met
    610                 615                 620

Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr
625                 630                 635                 640

Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala
                645                 650                 655

Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg
            660                 665                 670

Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys
        675                 680                 685

Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro
    690                 695                 700

Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala
705                 710                 715                 720

Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser
                725                 730                 735

Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala
            740                 745                 750

Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg
        755                 760                 765

Arg
```

(2) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 769 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..769
(D) OTHER INFORMATION: /note= "amino acids 1-560 and 565-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

```
Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1               5                  10                  15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
            20                  25                  30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
        35                  40                  45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
    50                  55                  60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65                  70                  75                  80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
                85                  90                  95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
            100                 105                 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
        115                 120                 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
    130                 135                 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145                 150                 155                 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
                165                 170                 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
            180                 185                 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
        195                 200                 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
    210                 215                 220
```

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225 230 235 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
245 250 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
260 265 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
275 280 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
290 295 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305 310 315 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
325 330 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
340 345 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
355 360 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
370 375 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385 390 395 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
405 410 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
420 425 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
435 440 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
450 455 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465 470 475 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro
485 490 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
500 505 510

Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg
515 520 525

Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
530 535 540

Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn
545 550 555 560

Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu
565 570 575

Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His
580 585 590

Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg
595 600 605

Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met
610 615 620

Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr
625 630 635 640

Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala
645 650 655

Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg
660 665 670

Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys
675 680 685

Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro
690 695 700

Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala
705 710 715 720

Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser
725 730 735

Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala
740 745 750

Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg
755 760 765

Arg

(2) INFORMATION FOR SEQ ID NO:40:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 769 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..769
(D) OTHER INFORMATION: /note= "amino acids 1-564 and 569-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1 5 10 15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
20 25 30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
35 40 45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
50 55 60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
65 70 75 80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
85 90 95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
100 105 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
115 120 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
130 135 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
145 150 155 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
165 170 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
180 185 190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
195 200 205

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
210 215 220

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro
225 230 235 240

His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp
245 250 255

Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser
260 265 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys
275 280 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser
290 295 300

Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His
305 310 315 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys
325 330 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp
340 345 350

Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln
355 360 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu
370 375 380

Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr
385 390 395 400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys
405 410 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu
420 425 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln
435 440 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala
450 455 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro
465 470 475 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro
485 490 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
500 505 510

Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg
515 520 525

Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
530 535 540

Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn
545 550 555 560

Asn Ile Asp Ser Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu
565 570 575

Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His
580 585 590

Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg
595 600 605

Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met
610 615 620

Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr
625 630 635 640

```
Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala
                645                 650                 655

Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg
            660                 665                 670

Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys
        675                 680                 685

Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro
    690                 695                 700

Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala
705                 710                 715                 720

Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser
                725                 730                 735

Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala
            740                 745                 750

Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg
        755                 760                 765

Arg
```

(2) INFORMATION FOR SEQ ID NO:41:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "amino acids 556-561 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

```
Arg Val Leu Lys Asn Asn
1               5
```

(2) INFORMATION FOR SEQ ID NO:42:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 434 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..434
(D) OTHER INFORMATION: /note= "entire amino acid sequence of C. elegans"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

```
Met Pro Glu Thr Asp Glu Glu Lys Val Arg Arg Tyr Thr Glu Cys Leu
1               5                  10                  15

Met Asn Gly Ile Asp Pro Lys Arg Ala Leu Lys Arg Leu Tyr Asp Leu
            20                  25                  30

Asn Val Ser Pro Glu Val Phe Lys Ser Ala Asp Thr Val Gln Cys Val
        35                  40                  45

Lys Arg Tyr Glu Ser Ser Pro Glu Leu Ala Lys Tyr Ala Lys Arg Val
    50                  55                  60

Arg Asp Lys Leu Leu Gly Gly Arg Lys Arg Glu Lys Gly Gly Gly Glu
65                  70                  75                  80

Asp Asp Ala Asp Ile Glu His Thr Ala Leu Lys Lys Ala Lys Lys Glu
                85                  90                  95

Glu Val Asn Leu Asp Glu Glu Phe Ala Glu Ala Met Lys Ser Gly Val
            100                 105                 110

Ser Ala Gln Ala Ser Ser Ala Pro Arg Ala Thr Val Asp Tyr Ser Lys
        115                 120                 125

Tyr Lys Val Val Lys Arg Val Glu Val Lys Val Glu Pro Lys Pro Glu
    130                 135                 140

Pro Val Asp Val His Glu Gln Gln Ala Ser Ser Ser Ser Met Ser Tyr
145                 150                 155                 160

Gln Arg Glu His Gln Lys Asp Tyr Ala Pro Val Val Pro Thr Cys Lys
                165                 170                 175

Pro Ser Gly Gln Pro Lys Lys Ala Ile Pro Gln Ser Lys Ser Leu His
            180                 185                 190

Ala Asp Glu Asn Met Phe Lys Pro Arg Lys Glu Arg Gln Lys Val Phe
        195                 200                 205

Ala Gly Arg Arg Lys Arg Val Gly Glu Gly Val Ser Thr Leu Val Ser
    210                 215                 220

Leu Cys Gln Thr Val Leu Met Ser His Ile Asp Met Ile Asp His Val
225                 230                 235                 240

Gly Ile Val Pro Phe Asp Leu Leu Lys Pro Val Leu Asp His Ala Ser
                245                 250                 255

Thr Asp Gln Leu Arg His Ile Leu Asp Val Asn Pro Met Leu Val Glu
            260                 265                 270

Asp Ala Asp Glu Met Phe His Glu Met Val Ser Arg Glu Phe Pro Lys
        275                 280                 285
```

Tyr Ala Asn Arg Glu Lys Ser Gly Trp Thr Trp Arg Glu Met Tyr Asp
290 295 300

Arg Leu Val Glu Lys Lys Gln Lys Lys Glu Asn Asp Lys Leu Glu Met
305 310 315 320

Leu Thr Ser Arg Ile Gly Lys Ser Asn Ser Ala Gln Ser Gln Gly Arg
325 330 335

Gln Thr Met Val Ile Asp Met Ala His Thr Arg Val Arg Ser Lys Ser
340 345 350

Phe Phe Asn Thr Val Lys Asp Ser Gln Val Lys Met Ser Ala Thr Pro
355 360 365

Ser Ala Leu Gln Leu Ser Gln Ala Arg Lys Asn Val Lys Ile Glu Gly
370 375 380

Lys Ala Gln Leu Arg Thr Ile Thr Pro Arg Gly Gly Gly Val Pro Ser
385 390 395 400

Thr Ser Arg Ser Arg Ser Asn Asn Asn Asn Asn Met Asn Asn Gly Leu
405 410 415

Val Val Lys Lys Thr Ala Pro Leu Met Ala Lys Cys Lys Lys Met Leu
420 425 430

Lys Arg

(2) INFORMATION FOR SEQ ID NO:43:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 143 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..143
(D) OTHER INFORMATION: /note= "amino acids 520-662 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

Glu Glu Ala Gly Phe Thr Gly Arg Arg Met Asn Ser Lys Met Gln Val
1 5 10 15

Tyr Ser Gly Ser Lys Cys Ala Tyr Leu Pro Lys Met Met Thr Leu His
20 25 30

Gln Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser Ile Phe Glu
35 40 45

Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu Glu Arg Cys
50 55 60

```
Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His Val Leu Ile
65                  70                  75                  80

Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg Asp Phe Lys
                85                  90                  95

Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met Tyr Leu Arg
            100                 105                 110

Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr Asn Asn Ile
        115                 120                 125

Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met
    130                 135                 140
```

(2) INFORMATION FOR SEQ ID NO:44:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 341 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..341
(D) OTHER INFORMATION: /note= "amino acids 94-434 of C. elegans"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

```
Lys Lys Glu Glu Val Asn Leu Asp Glu Glu Phe Ala Glu Ala Met Lys
1               5                   10                  15

Ser Gly Val Ser Ala Gln Ala Ser Ser Ala Pro Arg Ala Thr Val Asp
            20                  25                  30

Tyr Ser Lys Tyr Lys Val Val Lys Arg Val Glu Val Lys Val Glu Pro
        35                  40                  45

Lys Pro Glu Pro Val Asp Val His Glu Gln Gln Ala Ser Ser Ser Ser
    50                  55                  60

Met Ser Tyr Gln Arg Glu His Gln Lys Asp Tyr Ala Pro Val Val Pro
65                  70                  75                  80

Thr Cys Lys Pro Ser Gly Gln Pro Lys Lys Ala Ile Pro Gln Ser Lys
                85                  90                  95

Ser Leu His Ala Asp Glu Asn Met Phe Lys Pro Arg Lys Glu Arg Gln
            100                 105                 110

Lys Val Phe Ala Gly Arg Arg Lys Arg Val Gly Glu Gly Val Ser Thr
        115                 120                 125

Leu Val Ser Leu Cys Gln Thr Val Leu Met Ser His Ile Asp Met Ile
    130                 135                 140
```

```
Asp His Val Gly Ile Val Pro Phe Asp Leu Leu Lys Pro Val Leu Asp
145                 150                 155                 160

His Ala Ser Thr Asp Gln Leu Arg His Ile Leu Asp Val Asn Pro Met
                165                 170                 175

Leu Val Glu Asp Ala Asp Glu Met Phe His Glu Met Val Ser Arg Glu
            180                 185                 190

Phe Pro Lys Tyr Ala Asn Arg Glu Lys Ser Gly Trp Thr Trp Arg Glu
        195                 200                 205

Met Tyr Asp Arg Leu Val Glu Lys Lys Gln Lys Lys Glu Asn Asp Lys
    210                 215                 220

Leu Glu Met Leu Thr Ser Arg Ile Gly Lys Ser Asn Ser Ala Gln Ser
225                 230                 235                 240

Gln Gly Arg Gln Thr Met Val Ile Asp Met Ala His Thr Arg Val Arg
                245                 250                 255

Ser Lys Ser Phe Phe Asn Thr Val Lys Asp Ser Gln Val Lys Met Ser
            260                 265                 270

Ala Thr Pro Ser Ala Leu Gln Leu Ser Gln Ala Arg Lys Asn Val Lys
        275                 280                 285

Ile Glu Gly Lys Ala Gln Leu Arg Thr Ile Thr Pro Arg Gly Gly Gly
    290                 295                 300

Val Pro Ser Thr Ser Arg Ser Arg Ser Asn Asn Asn Asn Asn Met Asn
305                 310                 315                 320

Asn Gly Leu Val Val Lys Lys Thr Ala Pro Leu Met Ala Lys Cys Lys
                325                 330                 335

Lys Met Leu Lys Arg
            340
```

(2) INFORMATION FOR SEQ ID NO:45:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 233 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..233
(D) OTHER INFORMATION: /note= "amino acids 202-434 of C. elegans"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

```
Lys Glu Arg Gln Lys Val Phe Ala Gly Arg Arg Lys Arg Val Gly Glu
1               5                   10                  15
```

```
Gly Val Ser Thr Leu Val Ser Leu Cys Gln Thr Val Leu Met Ser His
            20                  25                  30

Ile Asp Met Ile Asp His Val Gly Ile Val Pro Phe Asp Leu Leu Lys
        35                  40                  45

Pro Val Leu Asp His Ala Ser Thr Asp Gln Leu Arg His Ile Leu Asp
    50                  55                  60

Val Asn Pro Met Leu Val Glu Asp Ala Asp Glu Met Phe His Glu Met
65                  70                  75                  80

Val Ser Arg Glu Phe Pro Lys Tyr Ala Asn Arg Glu Lys Ser Gly Trp
                85                  90                  95

Thr Trp Arg Glu Met Tyr Asp Arg Leu Val Glu Lys Lys Gln Lys Lys
            100                 105                 110

Glu Asn Asp Lys Leu Glu Met Leu Thr Ser Arg Ile Gly Lys Ser Asn
        115                 120                 125

Ser Ala Gln Ser Gln Gly Arg Gln Thr Met Val Ile Asp Met Ala His
    130                 135                 140

Thr Arg Val Arg Ser Lys Ser Phe Phe Asn Thr Val Lys Asp Ser Gln
145                 150                 155                 160

Val Lys Met Ser Ala Thr Pro Ser Ala Leu Gln Leu Ser Gln Ala Arg
                165                 170                 175

Lys Asn Val Lys Ile Glu Gly Lys Ala Gln Leu Arg Thr Ile Thr Pro
            180                 185                 190

Arg Gly Gly Gly Val Pro Ser Thr Ser Arg Ser Arg Ser Asn Asn Asn
        195                 200                 205

Asn Asn Met Asn Asn Gly Leu Val Val Lys Lys Thr Ala Pro Leu Met
    210                 215                 220

Ala Lys Cys Lys Lys Met Leu Lys Arg
225                 230
```

(2) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 98 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..98
(D) OTHER INFORMATION: /note= "amino acids 15-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

```
Asp Ala Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile
1               5                  10                  15

Val Lys Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu
            20                  25                  30

Ser Gly Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe
        35                  40                  45

Arg Glu Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr
    50                  55                  60

Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro
65                  70                  75                  80

Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu
                85                  90                  95

Asp Cys
```

(2) INFORMATION FOR SEQ ID NO:47:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 94 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..94
(D) OTHER INFORMATION: /note= "amino acids 19-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

```
Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys Arg Glu
1               5                  10                  15

His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly Pro Gly
            20                  25                  30

Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu Ile Pro
        35                  40                  45

Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys Val Arg
    50                  55                  60

Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala Pro Glu
65                  70                  75                  80

Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys
                85                  90
```

(2) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 90 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..90
(D) OTHER INFORMATION: /note= "amino acids 23-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

Ser Ser Asp Gly His Glu Phe Ile Val Lys Arg Glu His Ala Leu Thr
1 5 10 15

Ser Gly Thr Ile Lys Ala Met Leu Ser Gly Pro Gly Gln Phe Ala Glu
20 25 30

Asn Glu Thr Asn Glu Val Asn Phe Arg Glu Ile Pro Ser His Val Leu
35 40 45

Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys Val Arg Tyr Thr Asn Ser
50 55 60

Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu
65 70 75 80

Leu Leu Met Ala Ala Asn Phe Leu Asp Cys
85 90

(2) INFORMATION FOR SEQ ID NO:49:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 84 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..84
(D) OTHER INFORMATION: /note= "amino acids 29-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

Phe Ile Val Lys Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala
1 5 10 15

Met Leu Ser Gly Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val
20 25 30

Asn Phe Arg Glu Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr
35 40 45

Phe Thr Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu
50 55 60

Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn
65 70 75 80

Phe Leu Asp Cys

(2) INFORMATION FOR SEQ ID NO:50:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 56 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..56
(D) OTHER INFORMATION: /note= "amino acids 57-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

Thr Asn Glu Val Asn Phe Arg Glu Ile Pro Ser His Val Leu Ser Lys
1 5 10 15

Val Cys Met Tyr Phe Thr Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr
20 25 30

Glu Ile Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu
35 40 45

Met Ala Ala Asn Phe Leu Asp Cys
50 55

(2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 97 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..97
(D) OTHER INFORMATION: /note= "amino acids 1-97 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
50 55 60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65 70 75 80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
85 90 95

Pro

(2) INFORMATION FOR SEQ ID NO:52:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 83 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..83
(D) OTHER INFORMATION: /note= "amino acids 1-83 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
50 55 60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65 70 75 80

Val Arg Tyr

(2) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 102 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..102
(D) OTHER INFORMATION: /note= "amino acids 1-20 and 31-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Val Lys Arg Glu His Ala Leu Thr Ser Gly Thr Ile
20 25 30

Lys Ala Met Leu Ser Gly Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn
35 40 45

Glu Val Asn Phe Arg Glu Ile Pro Ser His Val Leu Ser Lys Val Cys
50 55 60

Met Tyr Phe Thr Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile
65 70 75 80

Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala
85 90 95

Ala Asn Phe Leu Asp Cys
100

(2) INFORMATION FOR SEQ ID NO:54:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 102 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..102
(D) OTHER INFORMATION: /note= "amino acids 1-30 and 41-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Thr Ile
20 25 30

Lys Ala Met Leu Ser Gly Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn
35 40 45

Glu Val Asn Phe Arg Glu Ile Pro Ser His Val Leu Ser Lys Val Cys
50 55 60

Met Tyr Phe Thr Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile
65 70 75 80

Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala
85 90 95

Ala Asn Phe Leu Asp Cys
100

(2) INFORMATION FOR SEQ ID NO:55:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 102 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..102
(D) OTHER INFORMATION: /note= "amino acids 1-40 and 51-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Gln Phe Ala Glu Asn Glu Thr Asn
35 40 45

Glu Val Asn Phe Arg Glu Ile Pro Ser His Val Leu Ser Lys Val Cys
50 55 60

Met Tyr Phe Thr Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile
65 70 75 80

Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala
85 90 95

Ala Asn Phe Leu Asp Cys
100

(2) INFORMATION FOR SEQ ID NO:56:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 102 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..102
(D) OTHER INFORMATION: /note= "amino acids 1-50 and 61-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

```
Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1               5                  10                  15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
            20                  25                  30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
        35                  40                  45

Pro Gly Asn Phe Arg Glu Ile Pro Ser His Val Leu Ser Lys Val Cys
    50                  55                  60

Met Tyr Phe Thr Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile
65                  70                  75                  80

Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala
                85                  90                  95

Ala Asn Phe Leu Asp Cys
            100
```

(2) INFORMATION FOR SEQ ID NO:57:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 102 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..102
(D) OTHER INFORMATION: /note= "amino acids 1-60 and 71-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

```
Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1               5                  10                  15
```

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Ser Lys Val Cys
50 55 60

Met Tyr Phe Thr Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile
65 70 75 80

Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala
85 90 95

Ala Asn Phe Leu Asp Cys
100

(2) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 102 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..102
(D) OTHER INFORMATION: /note= "amino acids 1-70 and 81-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
50 55 60

Ile Pro Ser His Val Leu Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile
65 70 75 80

Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala
85 90 95

Ala Asn Phe Leu Asp Cys
100

(2) INFORMATION FOR SEQ ID NO:59:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 102 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..102
(D) OTHER INFORMATION: /note= "amino acids 1-80 and 91-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
50 55 60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65 70 75 80

Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala
85 90 95

Ala Asn Phe Leu Asp Cys
100

(2) INFORMATION FOR SEQ ID NO:60:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 102 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..102
(D) OTHER INFORMATION: /note= "amino acids 1-90 and 101-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
50 55 60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65 70 75 80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Leu Glu Leu Leu Met Ala
85 90 95

Ala Asn Phe Leu Asp Cys
100

(2) INFORMATION FOR SEQ ID NO:61:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 112 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..112
(D) OTHER INFORMATION: /note= "amino acids 19-21 of Elongin C mutated to alanine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Ala Ala Ala Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
50 55 60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65 70 75 80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
85 90 95

Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys
100 105 110

(2) INFORMATION FOR SEQ ID NO:62:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 112 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..112
(D) OTHER INFORMATION: /note= "amino acids 22-24 of Elongin C mutated to alanine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ala Ala Ala Asp Gly His Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
50 55 60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65 70 75 80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
85 90 95

Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys
100 105 110

(2) INFORMATION FOR SEQ ID NO:63:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 112 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..112
(D) OTHER INFORMATION: /note= "amino acids 25-27 of Elongin C mutated to alanine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Ala Ala Ala Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
50 55 60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65 70 75 80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
85 90 95

Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys
100 105 110

(2) INFORMATION FOR SEQ ID NO:64:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 112 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..112
(D) OTHER INFORMATION: /note= "amino acids 28-30 of Elongin C mutated to alanine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Ala Ala Ala Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
50 55 60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65 70 75 80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
85 90 95

Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys
100 105 110

(2) INFORMATION FOR SEQ ID NO:65:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 112 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..112
(D) OTHER INFORMATION: /note= "amino acids 89-91 of Elongin C mutated to alanine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
50 55 60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65 70 75 80

Val Arg Tyr Thr Asn Ser Ser Thr Ala Ala Ala Glu Phe Pro Ile Ala
85 90 95

Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys
100 105 110

(2) INFORMATION FOR SEQ ID NO:66:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 112 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..112
(D) OTHER INFORMATION: /note= "amino acids 92-94 Elongin C mutated to alanine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
50 55 60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65 70 75 80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Ala Ala Ala Ile Ala
85 90 95

Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys
100 105 110

(2) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 112 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..112
(D) OTHER INFORMATION: /note= "amino acids 95-97 of Elongin C mutated to alanine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
50 55 60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65 70 75 80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ala Ala
85 90 95

Ala Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys
100 105 110

(2) INFORMATION FOR SEQ ID NO:68:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 112 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..112
(D) OTHER INFORMATION: /note= "amino acids 98-100 of Elongin C mutated to alanine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
50 55 60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65 70 75 80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
85 90 95

Pro Ala Ala Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys
100 105 110

(2) INFORMATION FOR SEQ ID NO:69:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 112 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..112
(D) OTHER INFORMATION: /note= "amino acids 101-103 of Elongin C mutated to alanine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

```
Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
            20                  25                  30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
        35                  40                  45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
    50                  55                  60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65                  70                  75                  80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
                85                  90                  95

Pro Glu Ile Ala Ala Ala Ala Leu Met Ala Ala Asn Phe Leu Asp Cys
            100                 105                 110
```

(2) INFORMATION FOR SEQ ID NO:70:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 112 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..112
(D) OTHER INFORMATION: /note= "amino acids 104-106 of Elongin C mutated to alanine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

```
Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1               5                   10                  15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
            20                  25                  30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
        35                  40                  45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
    50                  55                  60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65                  70                  75                  80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
                85                  90                  95

Pro Glu Ile Ala Leu Glu Leu Ala Ala Ala Ala Asn Phe Leu Asp Cys
            100                 105                 110
```

(2) INFORMATION FOR SEQ ID NO:71:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 112 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..112
(D) OTHER INFORMATION: /note= "amino acids 107-109 of Elongin C mutated to alanine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
20 25 30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
35 40 45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
50 55 60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65 70 75 80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
85 90 95

Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Ala Ala Leu Asp Cys
100 105 110

(2) INFORMATION FOR SEQ ID NO:72:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 112 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..112
(D) OTHER INFORMATION: /note= "amino acids 110-112 of Elongin C mutated to alanine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1 5 10 15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
20 25 30

```
Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
        35                  40                  45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
    50                  55                  60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65                  70                  75                  80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
                85                  90                  95

Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Ala Ala Ala
            100                 105                 110
```

(2) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 5 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..5
(D) OTHER INFORMATION: /note= "amino acids 18-22 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

```
Tyr Val Lys Leu Ile
1               5
```

(2) INFORMATION FOR SEQ ID NO:74:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 13 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..13
(D) OTHER INFORMATION: /note= "amino acids 18-30 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

```
Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile
1               5                   10
```

(2) INFORMATION FOR SEQ ID NO:75:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..24
(D) OTHER INFORMATION: /note= "amino acids 89-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

Glu Ile Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu
1 5 10 15

Met Ala Ala Asn Phe Leu Asp Cys
20

(2) INFORMATION FOR SEQ ID NO:76:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 52 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..52
(D) OTHER INFORMATION: /note= "amino acids 61-112 of Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

Asn Phe Arg Glu Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr
1 5 10 15

Phe Thr Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu
20 25 30

Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn
35 40 45

Phe Leu Asp Cys
50

(2) INFORMATION FOR SEQ ID NO:77:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 51 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

GAGTTGGTCA GTGCTCGCGT GGTCAAGAAC AGGCTTCAGT AGATCAAATG G 51

CLAIMS:

1. A substantially purified Elongin A fragment having transcriptional activation activity and capable of binding Elongin BC.

2. The substantially purified Elongin A fragment of claim 1 wherein said Elongin A fragment comprises an amino acid sequence as depicted in SEQ ID NO:16.

3. The substantially purified Elongin A fragment of claim 2 wherein said Elongin A fragment comprises an amino acid sequence as depicted in SEQ ID NO:2.

4. The substantially purified Elongin A fragment of claim 2 wherein said Elongin A fragment comprises an amino acid sequence as depicted in SEQ ID NO:3.

5. The substantially purified Elongin A fragment of claim 2 wherein said Elongin A fragment comprises an amino acid sequence as depicted in SEQ ID NO:4.

6. The substantially purified Elongin A fragment of claim 2 wherein said Elongin A fragment comprises an amino acid sequence as depicted in SEQ ID NO:5.

7. The substantially purified Elongin A fragment of claim 2 wherein said Elongin A fragment comprises an amino acid sequence as depicted in SEQ ID NO:6.

8. The substantially purified Elongin A fragment of claim 2 wherein said Elongin A fragment comprises an amino acid sequence as depicted in SEQ ID NO:17.

9. A nucleic acid comprising a nucleotide sequence encoding an Elongin A fragment having transcriptional activation activity and capable of binding to Elongin BC.

10. The nucleic acid of claim 9 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:16.

11. The nucleic acid of claim 10 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:2.

12. The nucleic acid of claim 10 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:3.

13. The nucleic acid of claim 10 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:4.

14. The nucleic acid of claim 10 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:5.

15. The nucleic acid of claim 10 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:6.

16. The nucleic acid of claim 10 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:17.

17. A substantially purified Elongin A having transcriptional activation activity and capable of binding to Elongin BC.

18. The substantially purified Elongin A of claim 17 comprising an amino acid sequence as depicted in SEQ ID NO:16.

19. The substantially purified Elongin A of claim 18 comprising an amino acid sequence as depicted in SEQ ID NO:2.

20. The substantially purified Elongin A of claim 18 comprising an amino acid sequence as depicted in SEQ ID NO:3.

21. The substantially purified Elongin A of claim 18 comprising an amino acid sequence as depicted in SEQ ID NO:4.

22. The substantially purified Elongin A of claim 18 comprising an amino acid sequence as depicted in SEQ ID NO:5.

23. The substantially purified Elongin A of claim 18 comprising an amino acid sequence as depicted in SEQ ID NO:6.

24. The substantially purified Elongin A of claim 18 comprising an amino acid sequence as depicted in SEQ ID NO:17.

25. A nucleic acid comprising a nucleotide sequence encoding an Elongin A having transcriptional activation activity and capable of binding to Elongin BC.

26. The nucleic acid of claim 25 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:16.

27. The nucleic acid of claim 26 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:2.

28. The nucleic acid of claim 26 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:3.

29. The nucleic acid of claim 26 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:4.

30. The nucleic acid of claim 26 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:5.

31. The nucleic acid of claim 26 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:6.

32. The nucleic acid of claim 26 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:17.

33. A substantially purified Elongin A comprising an amino acid sequence as depicted in SEQ ID NO:42.

34. A nucleic acid encoding an Elongin A comprising a nucleotide sequence encoding an amino acid sequence as depicted in SEQ ID NO:42.

35. A substantially purified Elongin C fragment having Elongin A activation activity and capable of binding to Elongin A and/or Elongin B.

36. The substantially purified Elongin C fragment of Claim 35 wherein said Elongin C fragment comprises an amino acid sequence as depicted in SEQ ID NO:46.

37. The substantially purified Elongin C fragment of Claim 35 wherein said Elongin C fragment comprises an amino acid sequence as depicted in SEQ ID NO:47.

38. The substantially purified Elongin C fragment of claim 35 wherein said Elongin C fragment comprises an amino acid sequence comprising the amino acid sequences as depicted in SEQ ID NO:10, SEQ ID NO:12, and SEQ ID NO:13.

39. A nucleic acid comprising a nucleotide sequence encoding an Elongin C fragment having Elongin A activation activity and capable of binding to Elongin A and/or Elongin B.

40. The nucleic acid of Claim 39, wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:46.

41. The nucleic acid of Claim 39, wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:47.

42. The nucleic acid of Claim 39, wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:10, SEQ ID NO:12, and SEQ ID NO:13.

43. A substantially purified Elongin C having Elongin activation activity and capable of binding to Elongin A and/or Elongin B.

44. The substantially purified Elongin of Claim 43, comprising an amino acid sequence as depicted in SEQ ID NO:46.

45. The substantially purified Elongin of Claim 43, comprising an amino acid sequence as depicted in SEQ ID NO:47.

46. The substantially purified Elongin C of claim 43 comprising an amino acid sequence comprising the amino acids sequences as depicted in SEQ ID NO:10, SEQ ID NO:12, and SEQ ID NO:13.

47. A nucleic acid comprising a nucleotide sequence encoding an Elongin C having Elongin A activation activity and capable of binding to Elongin A and/or Elongin B.

48. The nucleic acid of Claim 47, wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:46.

49. The nucleic acid of Claim 47, wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:47.

50. The nucleic acid of Claim 47, wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:10, SEQ ID NO:12, and SEQ ID NO:13.

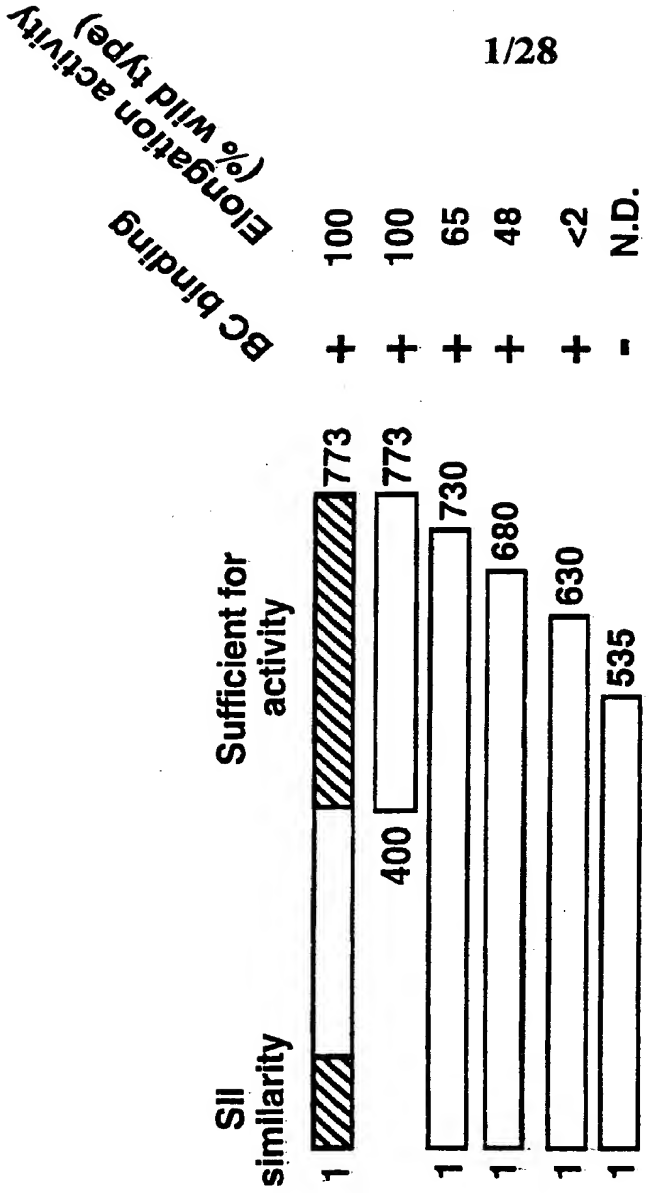
Elongation activity (% wild type)
BC binding
100
100
65
48
<2
N.D.
+
+
+
+
+
-
Sufficient for activity
SII similarity
773
773
730
680
630
535
400
1
1
1
1
1
1

Fig. 1A

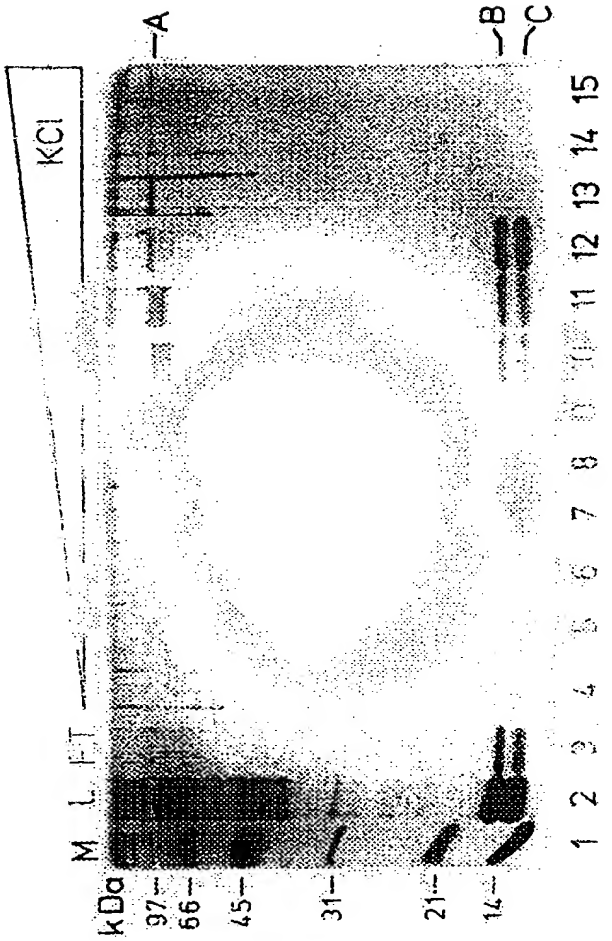

Fig. 1B

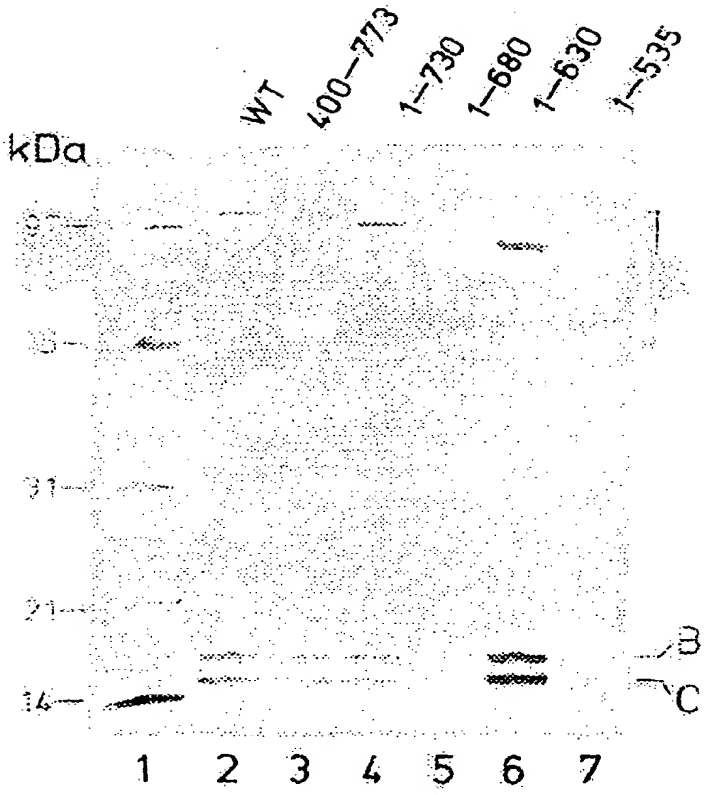

Fig. 1C

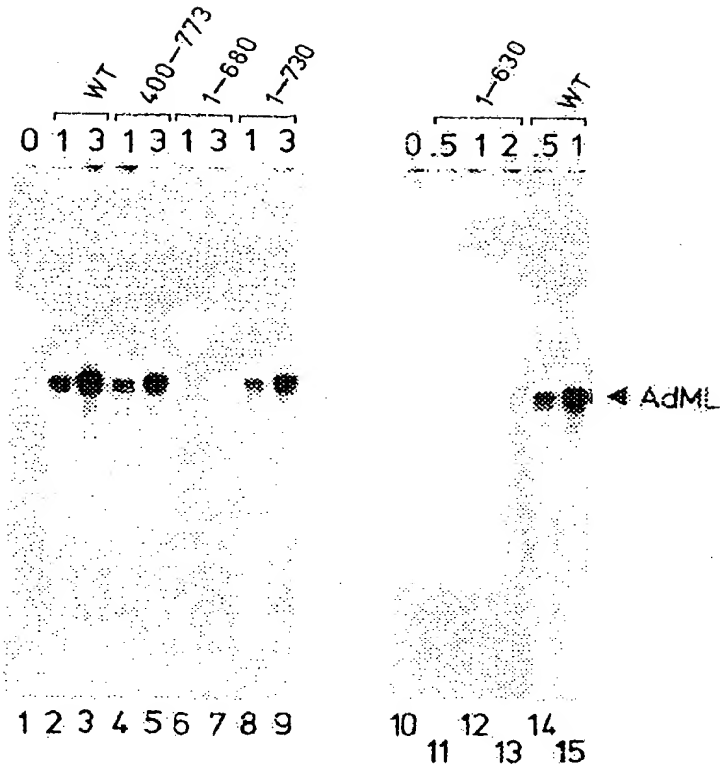
WT
400–773
1–680
1–730
0 1 3 1 3 1 3 1 3
1–630
WT
0.5 1 2 .5 1
AdML
1 2 3 4 5 6 7 8 9
10 11 12 13 14 15

Fig. 1D

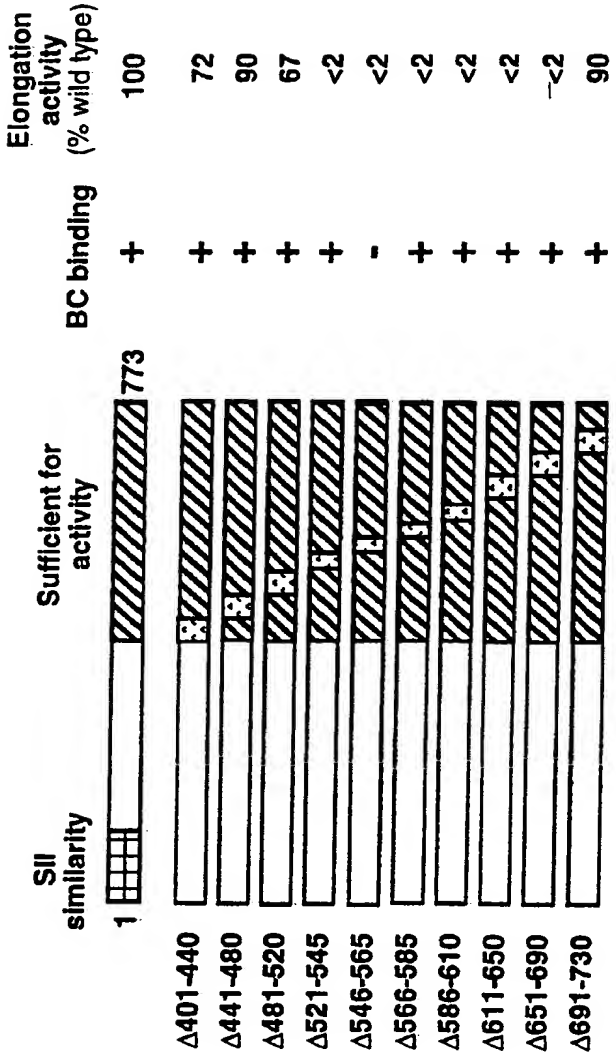
Elongation activity (% wild type)
BC binding
Sufficient for activity
SII similarity
1
773
Δ401-440
Δ441-480
Δ481-520
Δ521-545
Δ546-565
Δ566-585
Δ586-610
Δ611-650
Δ651-690
Δ691-730
100
72
90
67
<2
<2
<2
<2
<2
<2
90
+
+
+
+
+
-
+
+
+
+
+

Fig. 2A

6/28

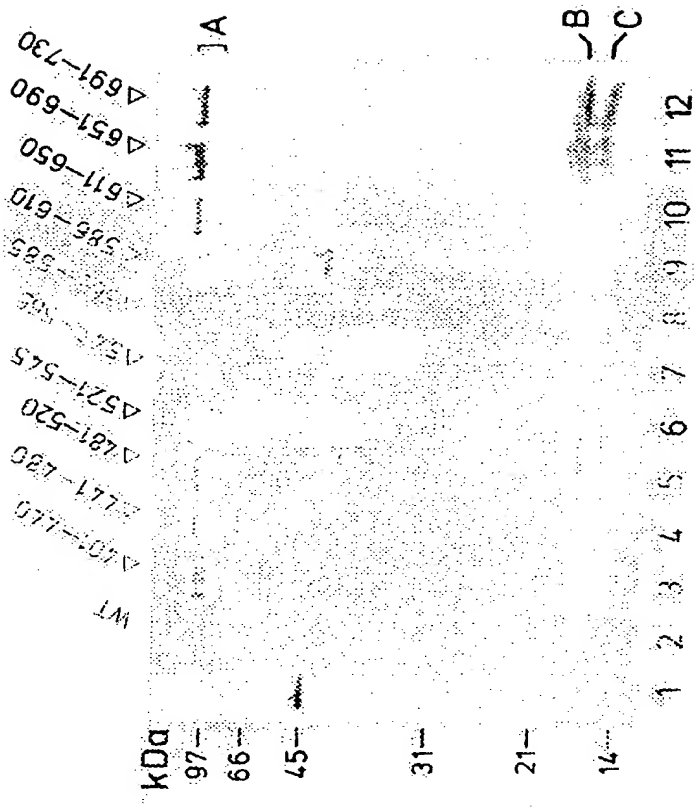
kDa
97
66
45
31
21
14
A
B
C
1 2 3 4 5 6 7 8 9 10 11 12
WT
Δ691–730
Δ651–690
Δ611–650
Δ581–620
Δ541–580
Δ521–545
Δ481–520
Δ441–480
Δ401–440

Fig. 2B

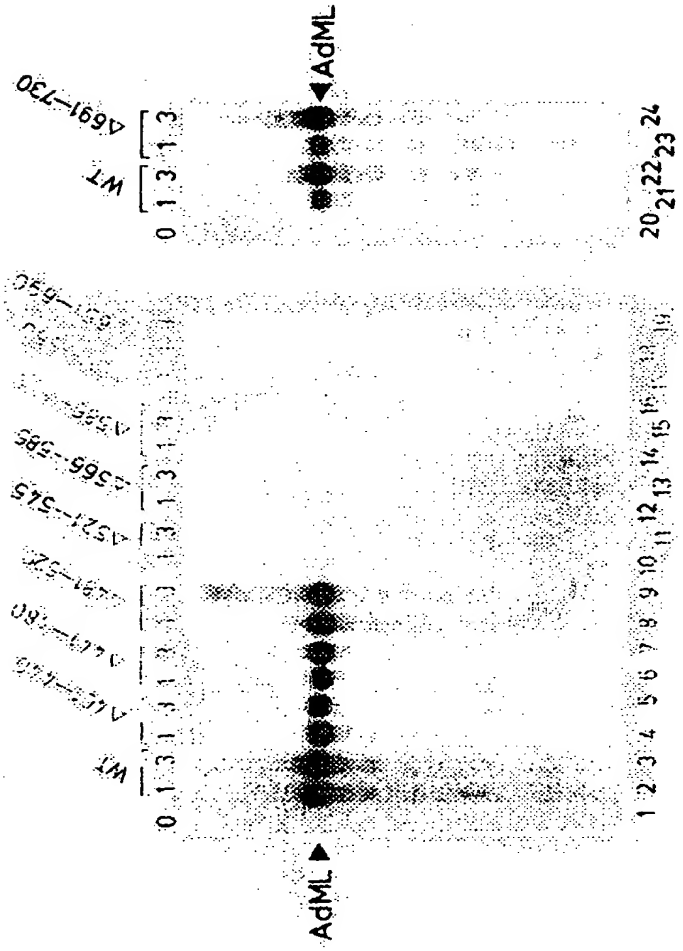
AdML
Δ691–730
WT
0 1 3 1 3
20 21 22 23 24
Δ565–585
Δ521–545
WT
0 1 3
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
AdML

Fig. 2C

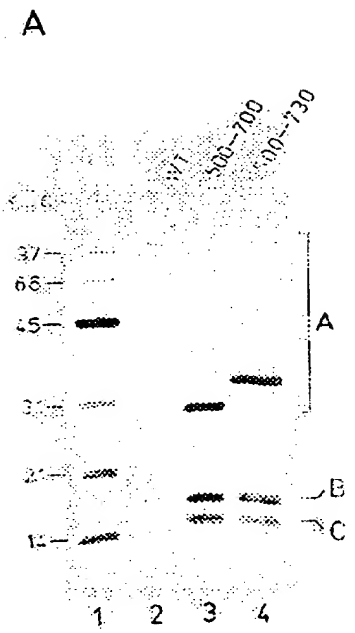
A
WT
500–700
500–730
97
66
45
A
B
C
1 2 3 4

Fig. 3A

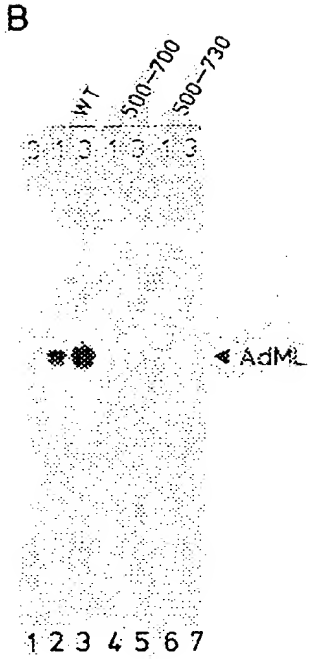
B
WT
500–700
500–730
AdML
1 2 3 4 5 6 7

Fig. 3B

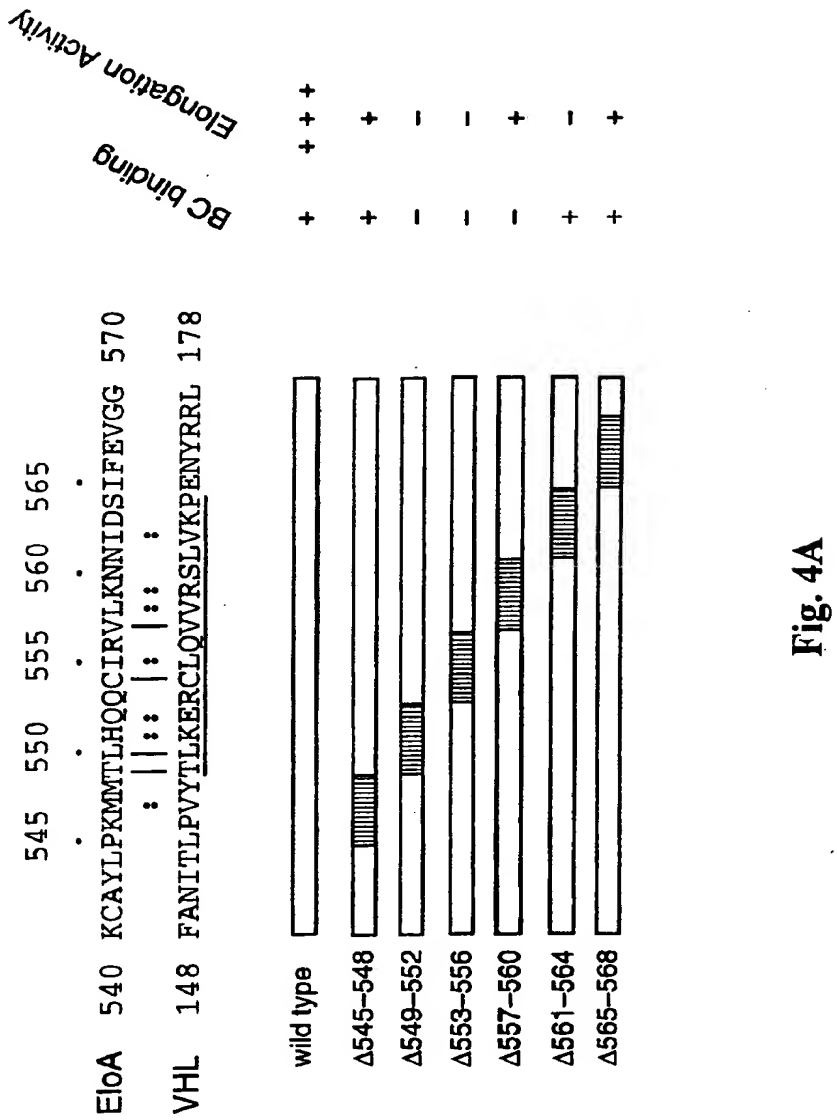
BC binding
Elongation Activity
wild type
Δ545–548
Δ549–552
Δ553–556
Δ557–560
Δ561–564
Δ565–568
545 550 555 560 565
EloA 540 KCAYLPKMMTLHQQCIRVLKNNIDSIFEVGG 570
VHL 148 FANITLPVYTLKERCLQVVRSLVKPENYRRL 178

Fig. 4A

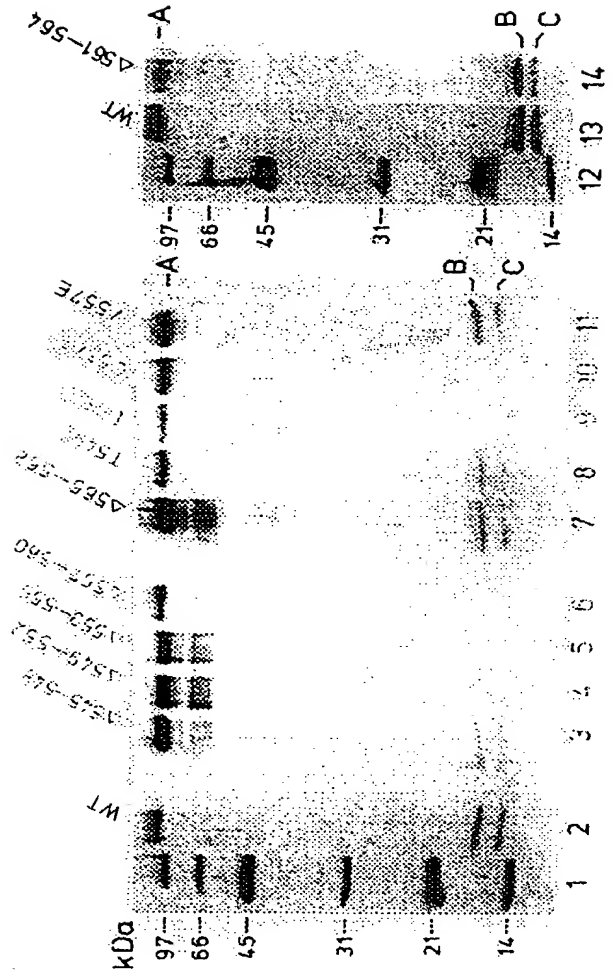

Fig. 4B

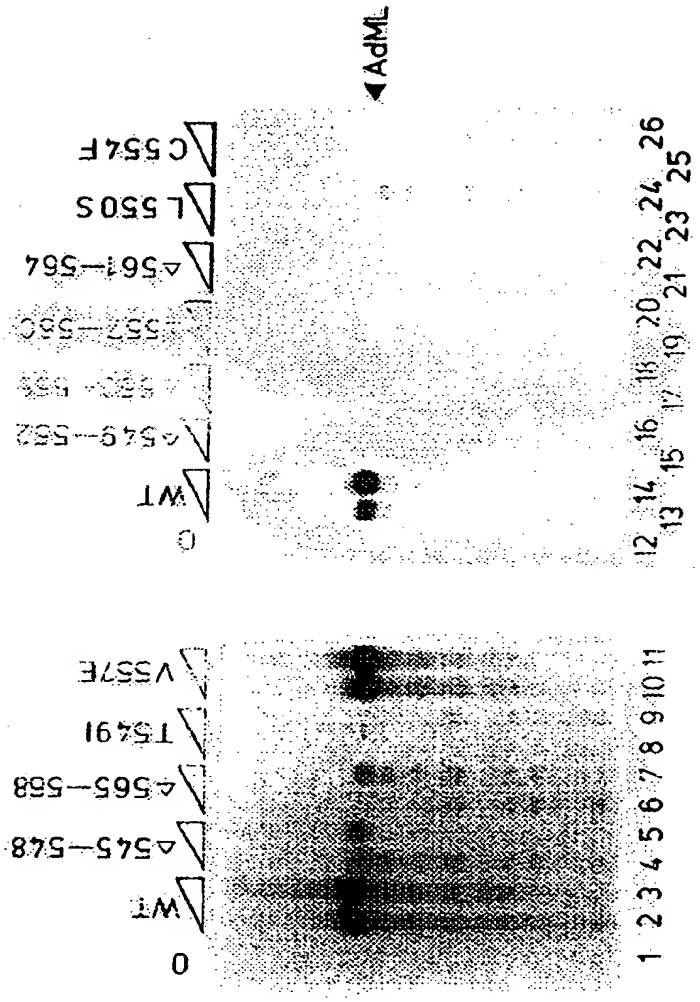
AdML
C554F
L550S
Δ561–564
Δ552–555
Δ549–552
WT
0
V557E
T549I
Δ565–568
Δ545–548
WT
0
1 2 3 4 5 6 7 8 9 10 11
12 13 14 15 16 17 18 19 20 21 22 23 24 25 26

Fig. 5A

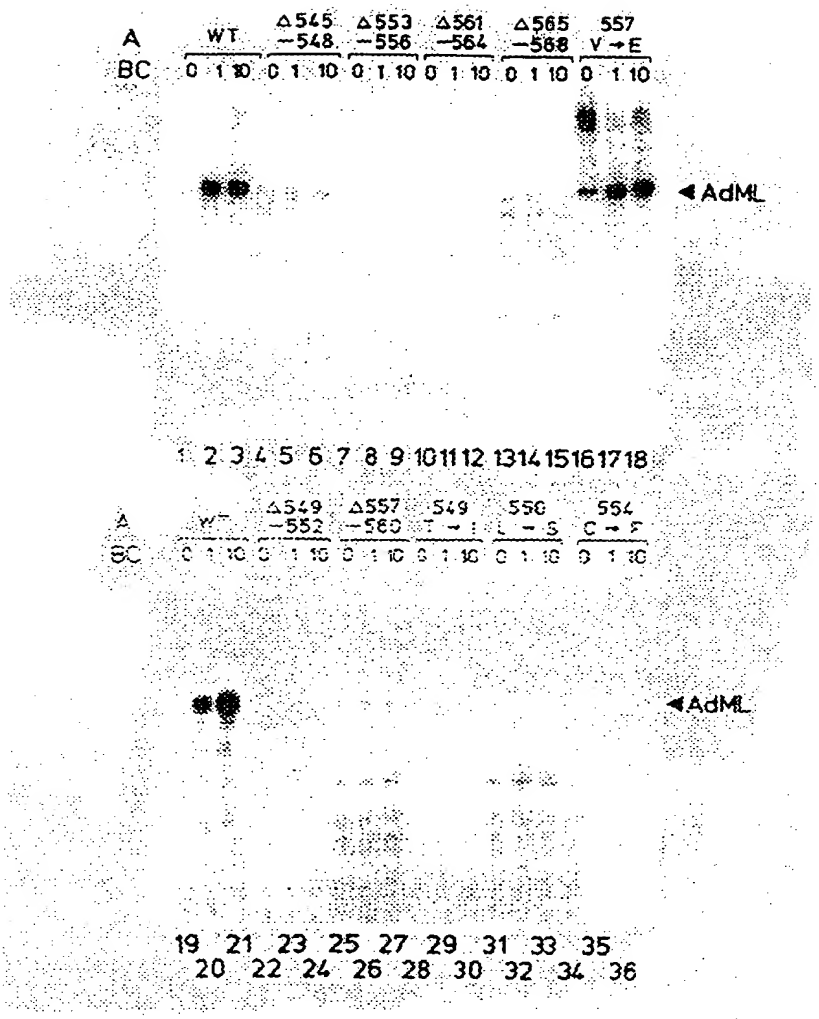
A
BC
WT
Δ545 −548
Δ553 −556
Δ561 −564
Δ565 −568
557 V → E
0 1 10 0 1 10 0 1 10 0 1 10 0 1 10 0 1 10
AdML
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
A
BC
WT
Δ549 −552
Δ557 −560
549 T → I
550 L → S
554 C → F
AdML
19 21 23 25 27 29 31 33 35
20 22 24 26 28 30 32 34 36

Fig. 5B

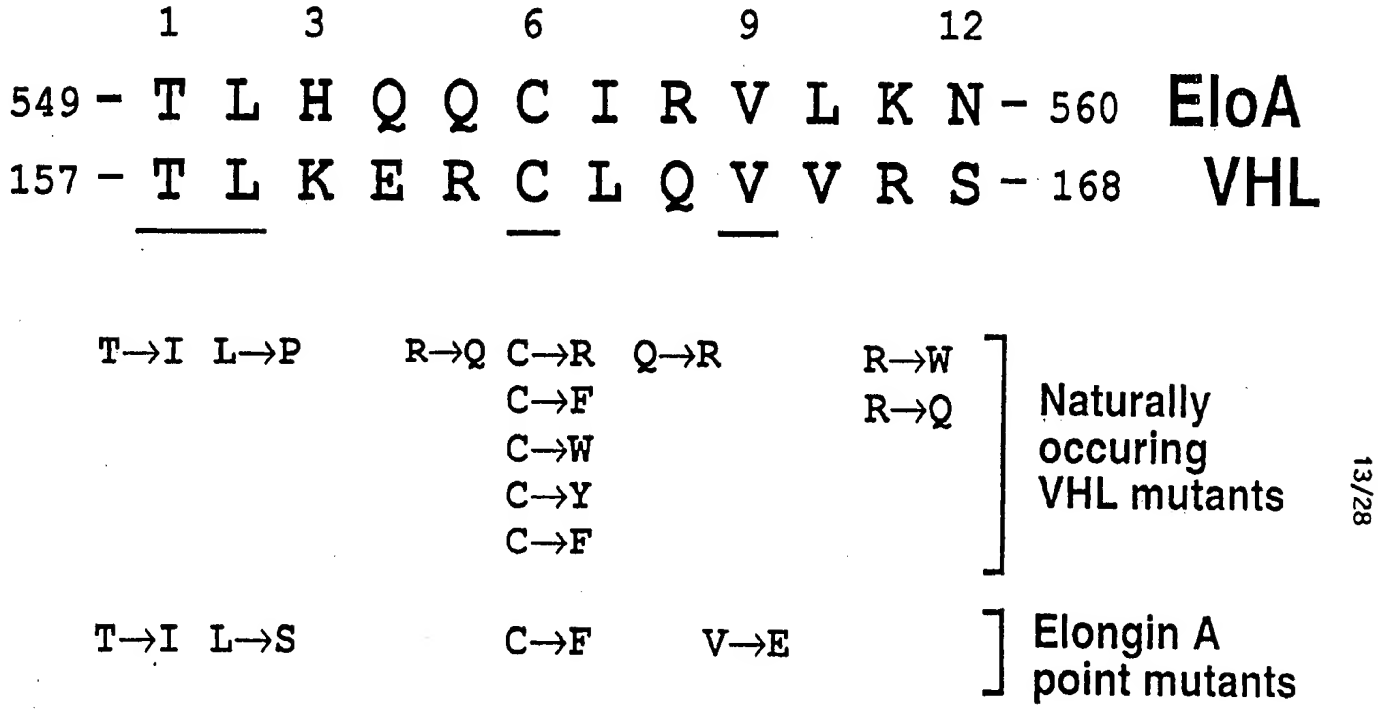
1 3 6 9 12
549 - T L H Q Q C I R V L K N - 560 EloA
157 - T L K E R C L Q V V R S - 168 VHL
T→I L→P
R→Q C→R Q→R
C→F
C→W
C→Y
C→F
R→W
R→Q
Naturally occuring VHL mutants
T→I L→S
C→F
V→E
Elongin A point mutants

Fig. 6

Rat
C. elegans
Rat
C. elegans
Rat
C. elegans
Rat
C. elegans
Rat
C. elegans
Rat
C. elegans
Rat
C. elegans
Rat
C. elegans
Rat
C. elegans
Rat
C. elegans
Rat
C. elegans
Rat
C. elegans
773
434

Fig. 7

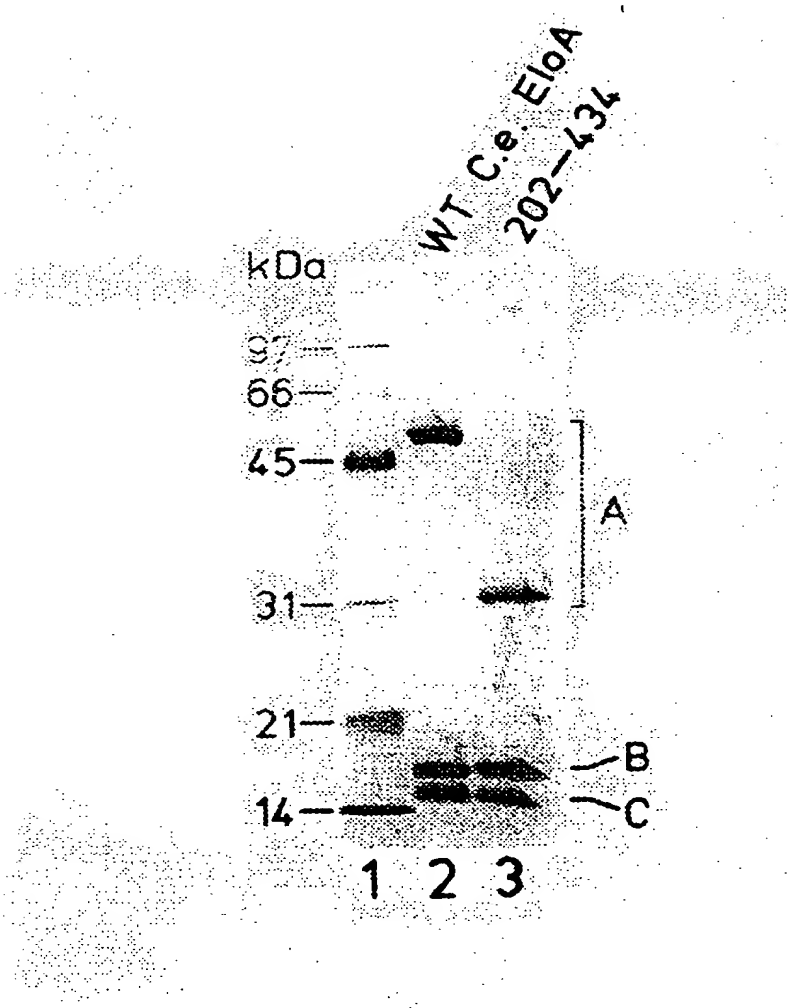

Fig. 8A

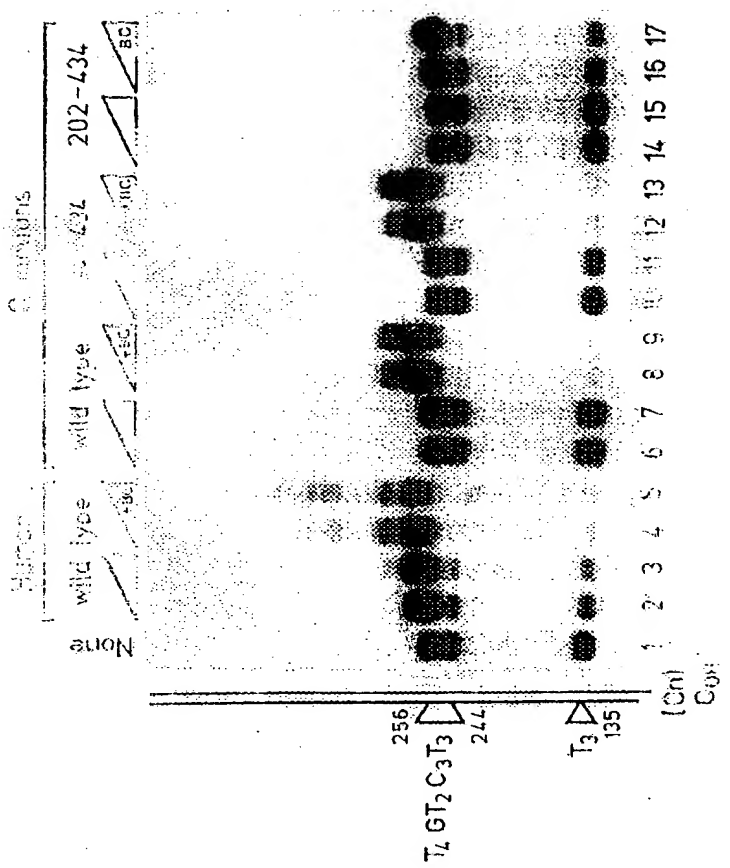
Enzyme
Competitors
None
wild type
wild type
202-434
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
(Cn)
Cpm
256
244
135
T4 GT2 C3 T3
T3

Fig. 8B

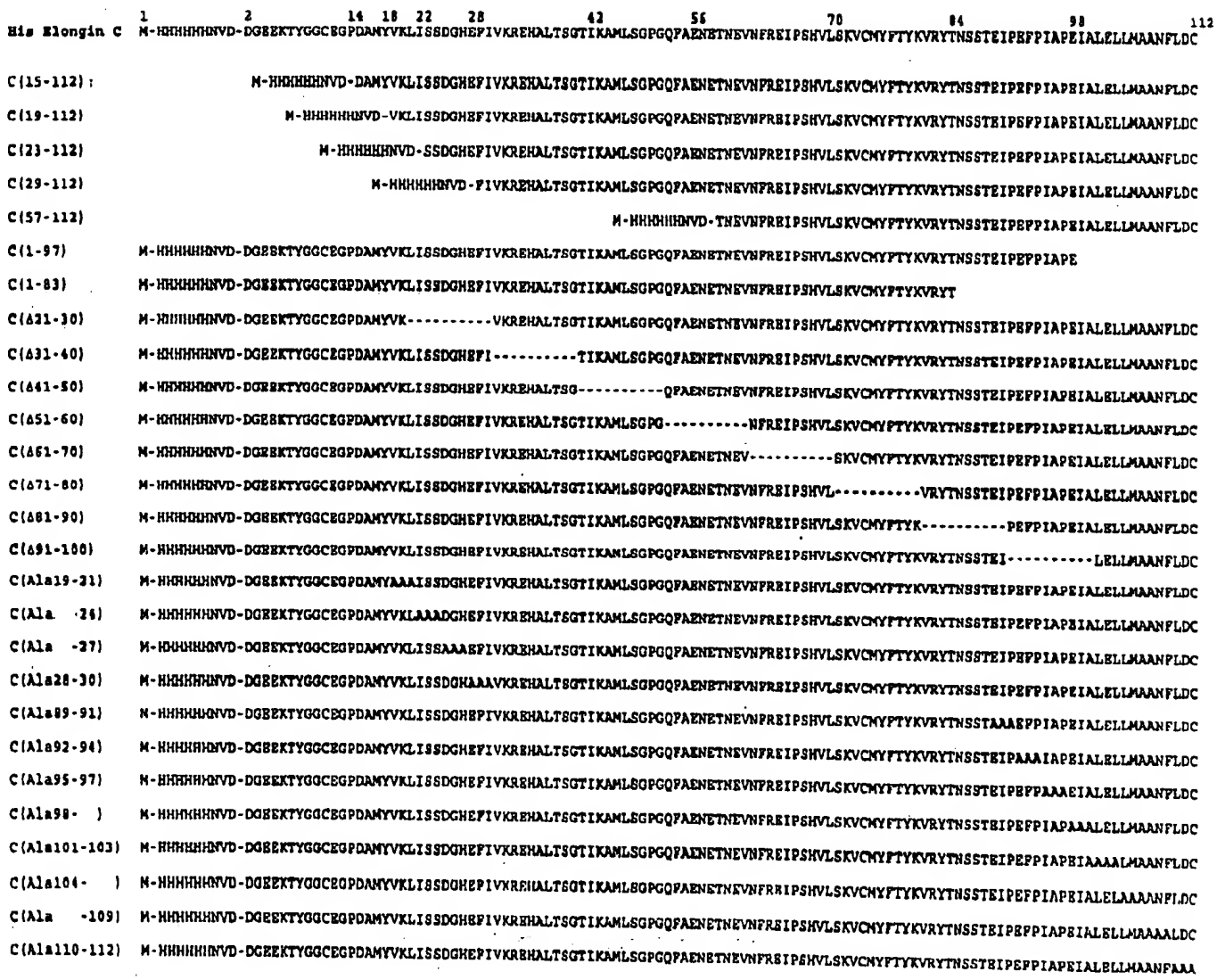
1 2 14 18 22 28 42 56 70 84 98 112
His Elongin C M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(15-112): M-HHHHHHNVD-DAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(19-112) M-HHHHHHNVD-VKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(23-112) M-HHHHHHNVD-SSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(29-112) M-HHHHHHNVD-FIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(57-112) M-HHHHHHNVD-TNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(1-97) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPE
C(1-83) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYT
C(Δ21-30) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVK----------VKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(Δ31-40) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFI----------TIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(Δ41-50) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSG----------QFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(Δ51-60) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPG----------NFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(Δ61-70) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEV----------SKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(Δ71-80) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVL----------VRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(Δ81-90) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYK----------PEFPIAPEIALELLMAANFLDC
C(Δ91-100) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEI----------LELLMAANFLDC
C(Ala19-21) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYAAAISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(Ala -26) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLAAADGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(Ala -27) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSAAAEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(Ala28-30) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHAAAVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFLDC
C(Ala89-91) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTAAAEFPIAPEIALELLMAANFLDC
C(Ala92-94) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPAAAIAPEIALELLMAANFLDC
C(Ala95-97) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPAAAEIALELLMAANFLDC
C(Ala98-) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPAAALELLMAANFLDC
C(Ala101-103) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIAAAALMAANFLDC
C(Ala104-) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELAAAANFLDC
C(Ala -109) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAAAALDC
C(Ala110-112) M-HHHHHHNVD-DGEEKTYGGCEGPDAMYVKLISSDGHEFIVKREHALTSGTIKAMLSGPGQFAENETNEVNFREIPSHVLSKVCMYFTYKVRYTNSSTEIPEFPIAPEIALELLMAANFAAA

Fig. 9

Fig. 10A

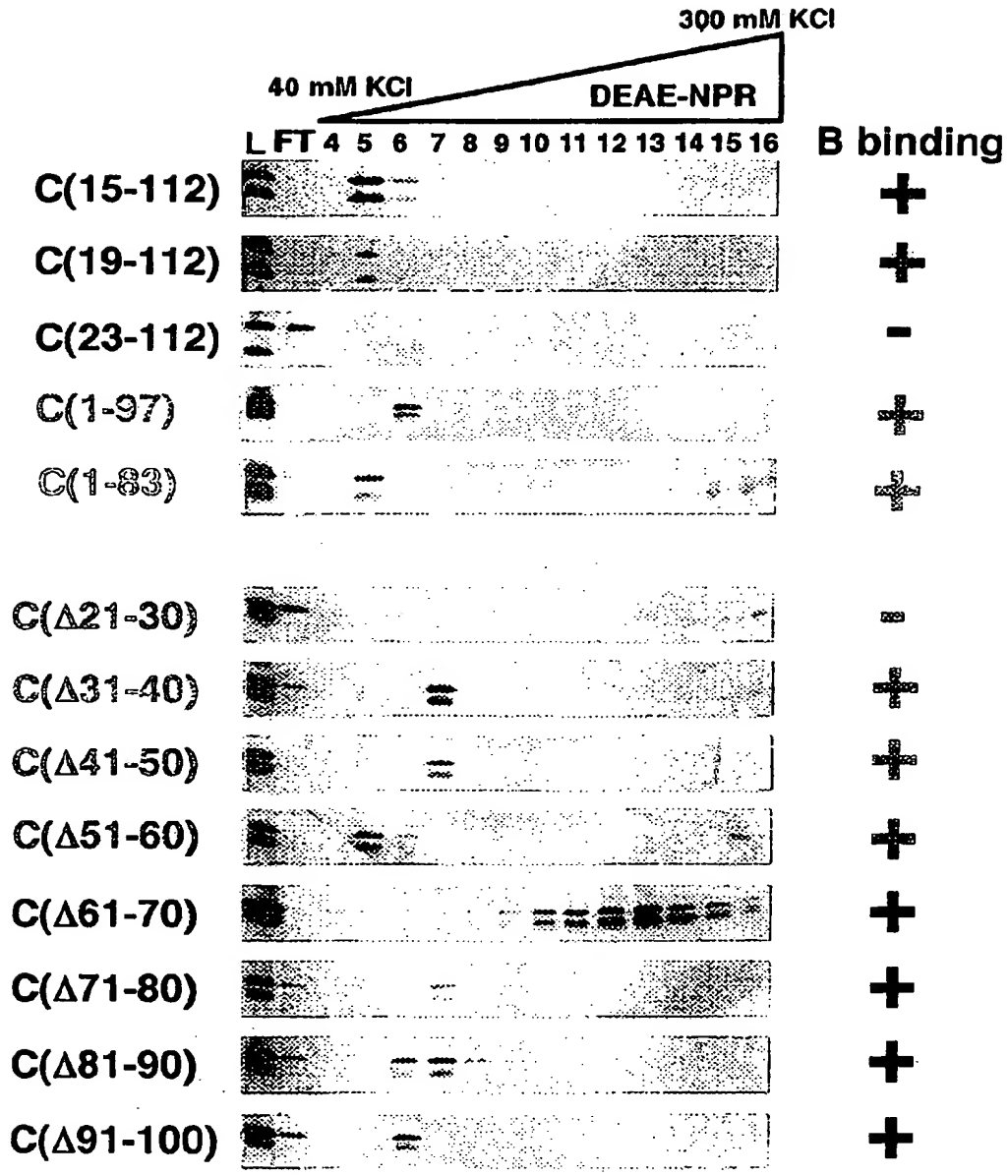
300 mM KCl
40 mM KCl
DEAE-NPR
L FT 4 5 6 7 8 9 10 11 12 13 14 15 16
B binding
C(15-112)
C(19-112)
C(23-112)
C(1-97)
C(1-83)
C(Δ21-30)
C(Δ31-40)
C(Δ41-50)
C(Δ51-60)
C(Δ61-70)
C(Δ71-80)
C(Δ81-90)
C(Δ91-100)

Fig. 10B

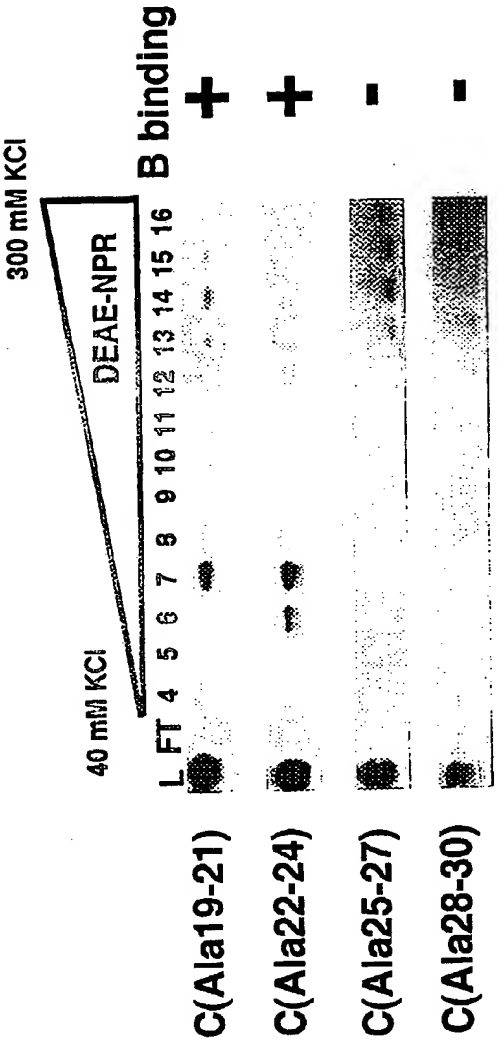
B binding
+
+
-
-
300 mM KCl
DEAE-NPR
40 mM KCl
L FT 4 5 6 7 8 9 10 11 12 13 14 15 16
C(Ala19-21)
C(Ala22-24)
C(Ala25-27)
C(Ala28-30)

Fig. 10C

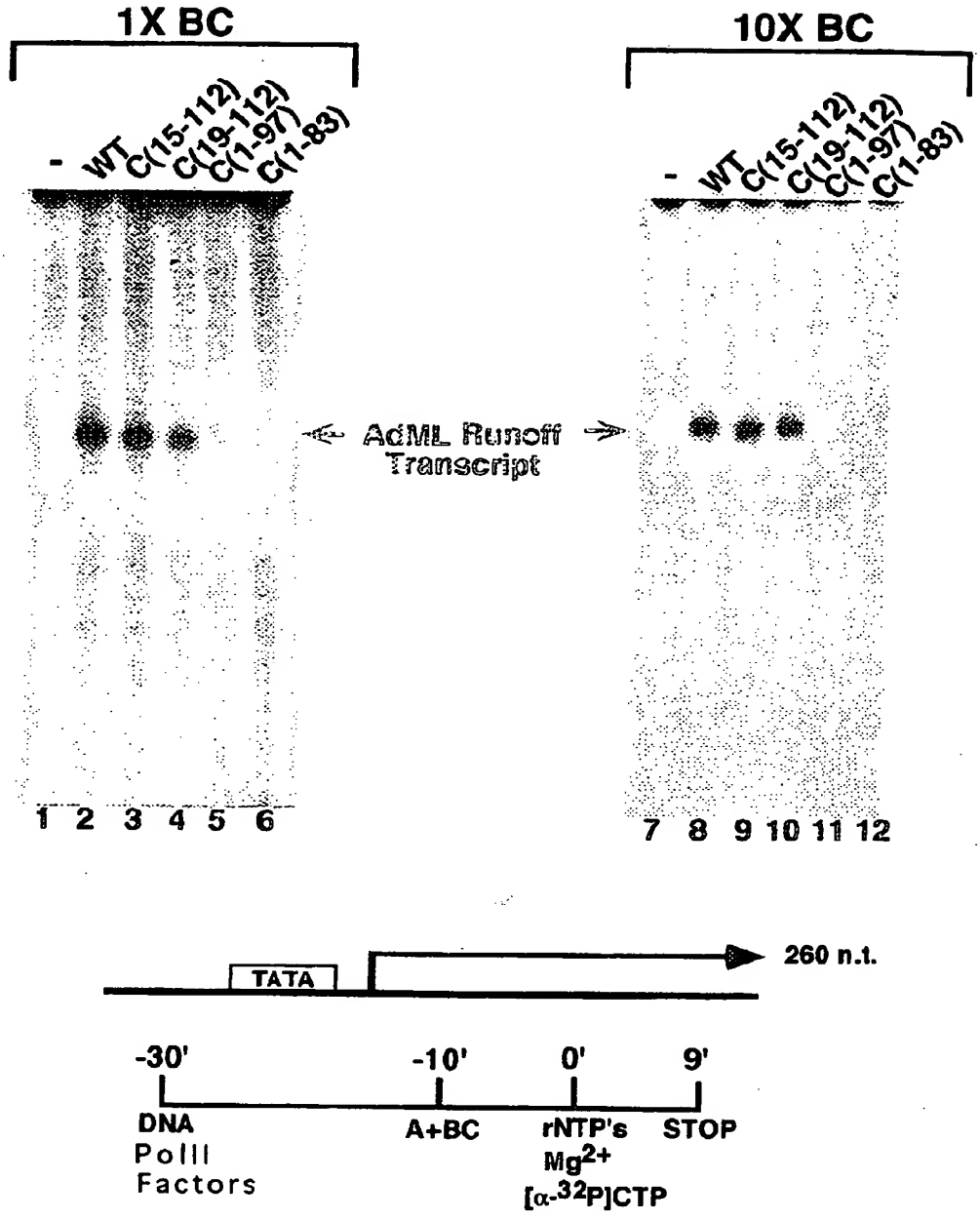
1X BC
10X BC
- WT C(15-112) C(19-112) C(1-97) C(1-83)
- WT C(15-112) C(19-112) C(1-97) C(1-83)
AdML Runoff Transcript
1 2 3 4 5 6
7 8 9 10 11 12
TATA
260 n.t.
-30'
-10'
0'
9'
DNA PolII Factors
A+BC
rNTP's Mg2+ [α-32P]CTP
STOP

Fig. 11A

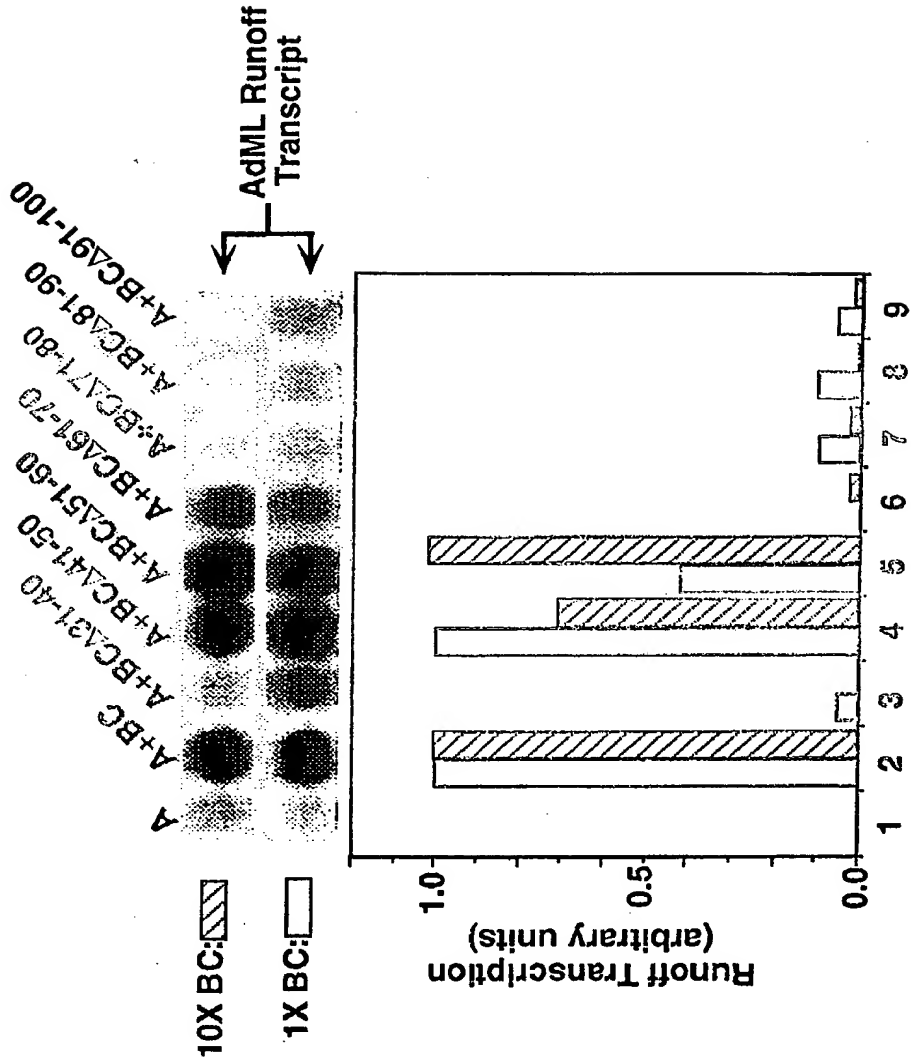
AdML Runoff Transcript
A
A+BC
A+BCΔ31-40
A+BCΔ41-50
A+BCΔ51-60
A+BCΔ61-70
A+BCΔ71-80
A+BCΔ81-90
A+BCΔ91-100
10X BC:
1X BC:
Runoff Transcription (arbitrary units)
0.0
0.5
1.0
1
2
3
4
5
6
7
8
9

Fig. 11B

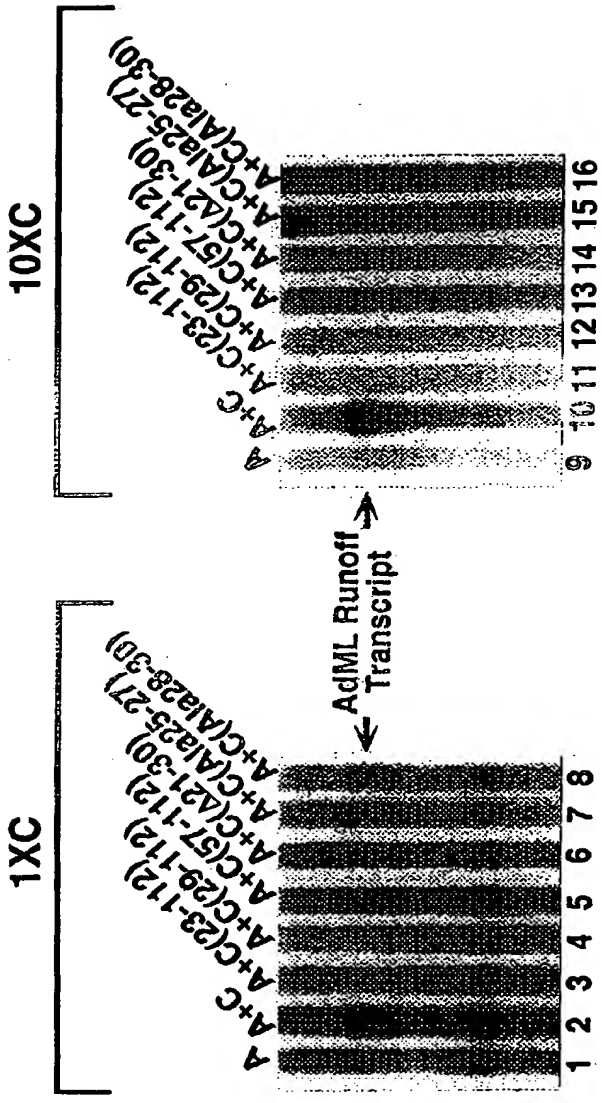
10XC
A
A+C
A+C(23-112)
A+C(29-112)
A+C(57-112)
A+C(A21-30)
A+C(A1a25-27)
A+C(A1a28-30)
9 10 11 12 13 14 15 16
AdML Runoff Transcript
1XC
A
A+C
A+C(23-112)
A+C(29-112)
A+C(57-112)
A+C(A21-30)
A+C(A1a25-27)
A+C(A1a28-30)
1 2 3 4 5 6 7 8

Fig. 12A

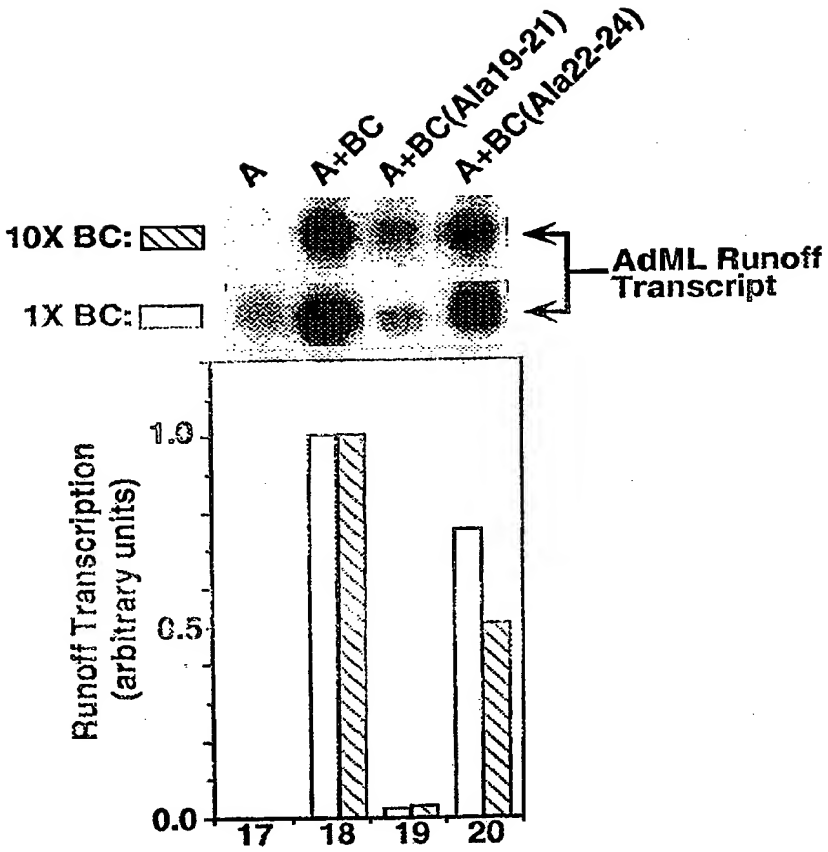
A
A+BC
A+BC(Ala19-21)
A+BC(Ala22-24)
10X BC:
1X BC:
AdML Runoff Transcript
Runoff Transcription (arbitrary units)
1.0
0.5
0.0
17
18
19
20

Fig. 12B

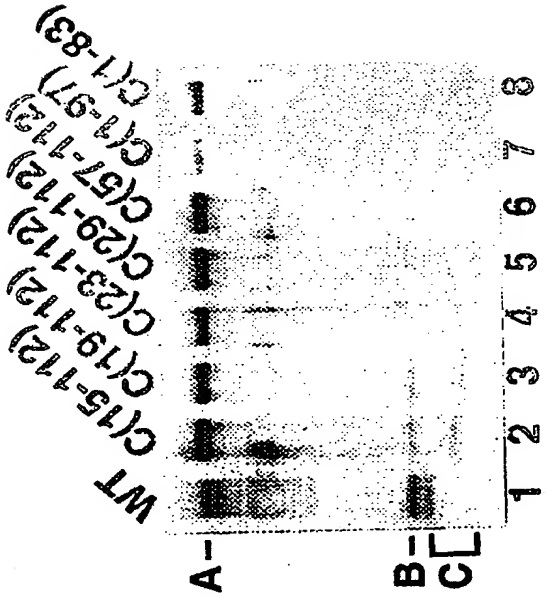
WT
C(15-112)
C(19-112)
C(23-112)
C(29-112)
C(57-112)
C(9-97)
C(1-83)
A
B
CL
1
2
3
4
5
6
7
8

Fig. 13

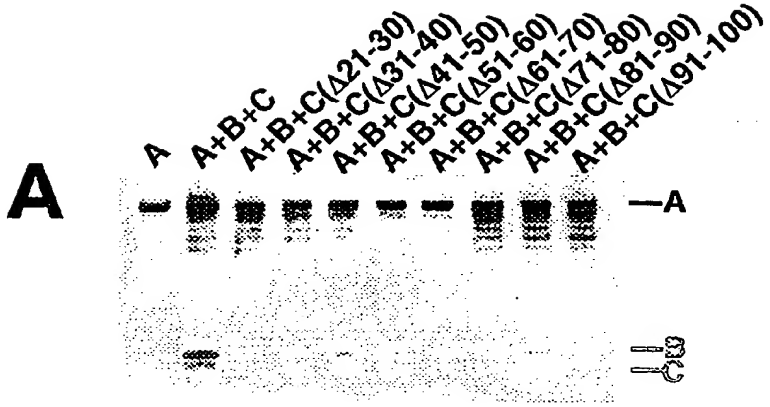

Fig. 14A

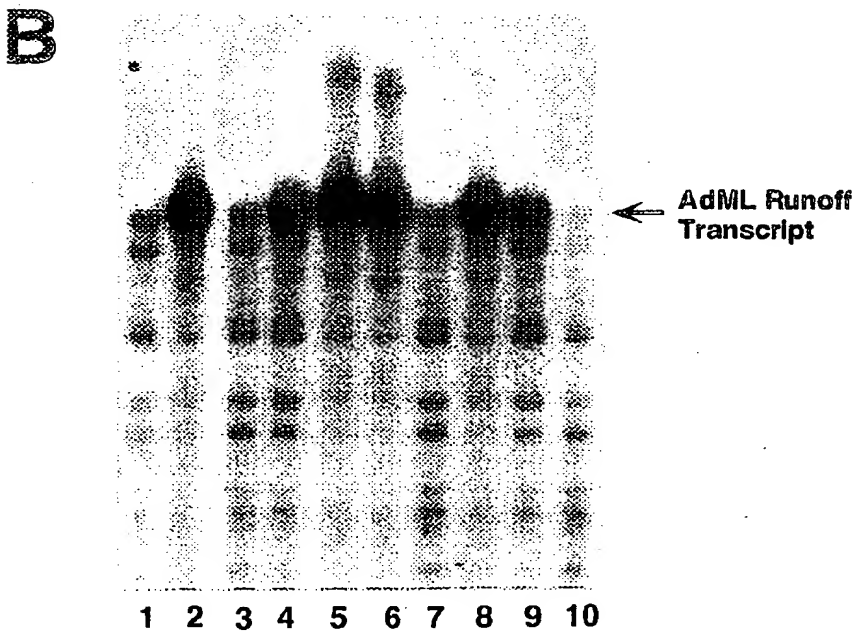

Fig. 14B

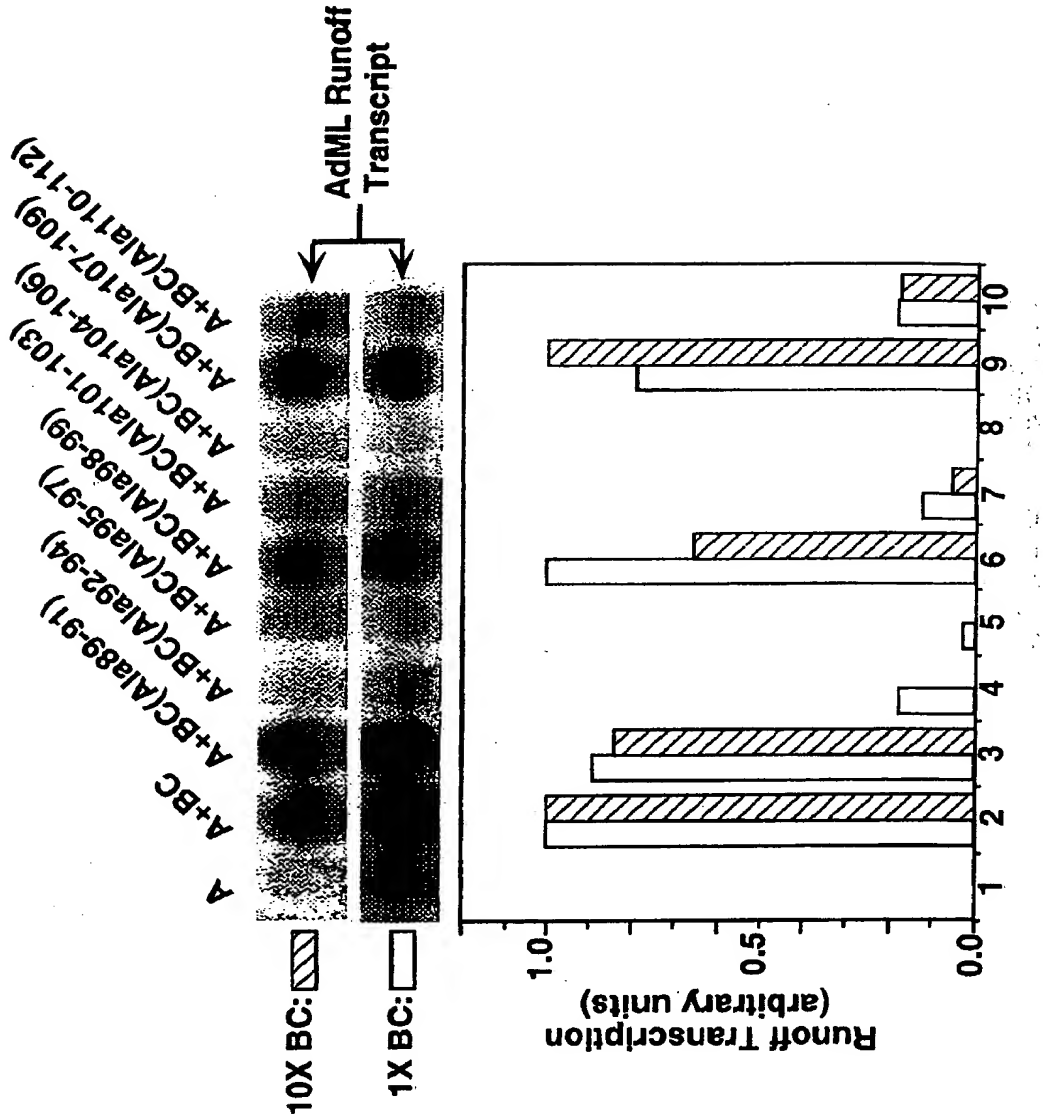
AdML Runoff Transcript
A
A+BC
A+BC(Ala89-91)
A+BC(Ala92-94)
A+BC(Ala95-97)
A+BC(Ala98-99)
A+BC(Ala101-103)
A+BC(Ala104-106)
A+BC(Ala107-109)
A+BC(Ala110-112)
10X BC:
1X BC:
Runoff Transcription (arbitrary units)
0.0
0.5
1.0
1
2
3
4
5
6
7
8
9
10

Fig. 15

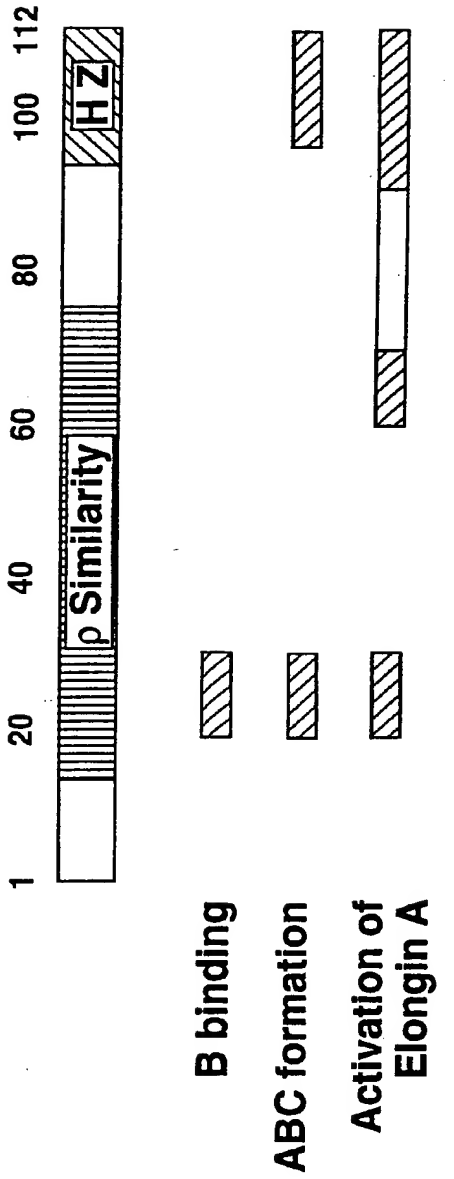
1
20
40
60
80
100
112
ρ Similarity
H Z
B binding
ABC formation
Activation of Elongin A

Fig. 16

INTERNATIONAL SEARCH REPORT

Int tional Application No
PCT/US 97/17992

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C07K14/47 C07K14/435

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 655 498 A (OKLAHOMA MED RES FOUND) 31 May 1995 see abstract see page 25 - page 27 see page 28 - page 29	17-34, 43-50
Y		1-16, 35-42
X	ASO T. ET AL.: "Elongin (SIII): a multisubunit regulator of elongation by RNA polymerase II." SCIENCE, vol. 269, 8 September 1995, pages 1439-1443, XP002023196 see abstract see page 1443; figure 6	1,2

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 February 1998	25/02/1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Lejeune, R

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INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/US 97/17992

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication,where appropriate of the relevant passages	Relevant to claim No.
X	DATABASE SWISSPROT YRL4_CAEEL (AC Q09413), 1 October 1996 SWINBURNE J.: "HYPOTHETICAL 49.2 KD PROTEIN R03D7.4 IN CHROMOSOME II" XP002055270 see sequence	33,34
Y	TAN S. ET AL.: "Dissection of transcription factor TFIIF functional domains required for initiation and elongation." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 92, 20 June 1995, pages 6042-6046, XP002055269 see abstract see page 6043; figure 1	1-16, 35-42
P,X	WO 97 09426 A (OKLAHOMA MED RES FOUND) 13 March 1997 see page 63 - page 64 see page 70 - page 72 see page 42, line 25 - line 30	1-34, 43-50
P,X	ASO T. ET AL.: "The inducible elongin A elongation activation domain: structure, function and interaction with the elongin BC complex." THE EMBO JOURNAL, vol. 15, no. 20, 15 October 1996, pages 5557-5566, XP002055267 see the whole document	1-34
P,X	TAKAGI Y. ET AL.: "Characterization of elongin C functional domains required for interaction with elongin B and activation of elongin A." THE JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 271, no. 41, 11 October 1996, pages 25562-25568, XP002055268 see the whole document	35-50

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